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BRITISH MEDICAL JOURNAL

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ADVANCED EXTRAUTERINE PREGNANCY

BY

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"The palpable obscure."—Milton.

Occasional cases of advanced abdominal pregnancy have excited interest and curiosity for many centuries. The rarity of the condition and its inherent drama have led to a large proportion of these cases having been put on record. Ware (1948) found that 311 cases had been reported between 1809 and 1933, and he collected 249 recorded cases between 1933 and 1946. Like early ectopic pregnancies, advanced extrauterine pregnancies are less common in highly organized communities than in underdeveloped ones, and many experienced obstetricians have never encountered the condition. During the first six years after the obstetrics wards at the University College Hospital, Jamaica, opened, 10 extrauterine pregnancies of over 20 weeks' gestation were encountered among 9,303 deliveries, an incidence of 1 in 930. All these cases were cared for by obstetricians who had been trained in other parts of the world and had not been faced with the problems of this condition until they came to Jamaica. It has seemed to us worth while to put our cases on record and to give an account of the difficulties we and our colleagues encountered in the diagnosis and management of this complication of pregnancy.

Points Emerging from the Literature

We do not propose to review the numerous reports of small series and individual cases. The literature includes several major contributions to the knowledge of this difficult condition, and from them several points emerge on which there appears to be general agreement.

1. *Advanced Extrauterine Pregnancy is Dangerous for Both Mother and Child.*—Maternal mortality ranges from nil among the eight cases reported by Yahia and Montgomery (1956) and the 11 cases of Zuspan *et al.* (1957) to 20% and 30% respectively in the series of Cross *et al.* (1951) and Ware (1948). We consider ourselves extremely fortunate to be able to report 10 cases with no maternal death. The outlook for the foetus is even gloomier, but in many reported cases, as in four from our own series, the foetus had died before the diagnosis of extrauterine pregnancy was made. Foetal mortalities ranging from 90% (Charlewood and Culiner, 1955) to 60% (Yahia and Montgomery, 1956) have been reported. Again we have been fortunate that in 5 of our 10 patients the foetus was alive and mature enough to be viable; four of these children survive, and one died of prematurity after a successful delivery.

2. *The Diagnosis is Difficult.*—This often leads to delay, and delay in diagnosis in turn increases the risk, at least to the foetus. As King (1954) has pointed out, the diagnosis is often missed simply because this rare condition is not considered.

3. *The Placenta is a Source of Danger.*—There seems to be a majority opinion in favour of leaving the placenta *in situ*, for fear of provoking uncontrollable haemorrhage, except in occasional cases when it is so situated that it can be removed easily and safely. According to King, the method of dealing with the placenta was considered by Lawson Tait (1888) to be "the crux of the discussion." Tait believed that the placenta should be removed whenever possible and only rarely left *in situ*. Beck (1919) agreed that removal of the placenta was best, but maintained that ligation of the vessels supplying the placental site should precede all attempts at removal; when this could not be achieved the placenta should be left undisturbed. Of more recent writers some advocate removal of the placenta in every possible case (Barrett, 1952; Hibbard, 1957), while a few are convinced that removal of the placenta is so dangerous that it should never be attempted (Cross *et al.*, 1951; Barber and Rathbun, 1958). In each of our cases the placenta has been removed, but in six hysterectomy was necessary in order to do this. The reasons for our course of action are discussed in detail below.

Our 10 cases are summarized in Table I. They are arranged in order of duration of pregnancy. Two were non-viable by dates; three were well past term and the babies were dead when the diagnosis was made. Four of the five remaining infants survive, while one died after delivery. The difficulties encountered in the diagnosis and management of these patients are considered.

Diagnosis

According to King success in diagnosis depends on considering (*a*) the possibility of pregnancy and (*b*) the possibility that the pregnancy is extrauterine. We have been interested in the value of the various points in the history and physical findings that have been described as aiding in this often difficult diagnosis.

History

Three of our 10 cases gave a history of *previous ectopic pregnancy*. In two of these we found that the advanced extrauterine pregnancy arose on the same side as the previous tubal pregnancy, which had been treated by partial salpingectomy.

Much importance has been placed upon the *history of abdominal pain early in pregnancy*. Only two of our patients gave this history, and these happened to be the two in whom the diagnosis was made before the 29th week of pregnancy. The other patients, whose condition was diagnosed later in pregnancy, gave histories of no pain whatsoever or of mild pain gradually increasing after the second half of pregnancy.

The one patient diagnosed at term (Case 7) and two of the three with post-mature dead foetuses gave a convincing history of *spurious labour* at or near term, without previous pain. In Case 8 this helped in reaching a diagnosis.

Vaginal bleeding in early pregnancy is said to be common among cases of extrauterine pregnancy, varying from 25% in King's series to 87% among the cases of Yahia and Montgomery. Only one of our patients (Case 1) gave a history of bleeding in early pregnancy. Bleeding in later pregnancy occurred in three patients (Cases 2, 9, and 10), but in each it was associated with foetal death and probably constituted part of a spurious labour. In the two cases (Nos. 9 and 10) first seen many weeks after the foetus had died it seemed that menstruation had become re-established.

These cases also support the suggestion of Cross *et al.* (1951) that *prolonged retention of a dead foetus* may be an indication of extrauterine pregnancy, and that this becomes practically certain if the pregnancy continues longer than two months after death of the foetus.

Physical Findings

Ease of Palpation of Foetal Parts.—In some cases the foetal parts can be felt much more easily through the thin gestation sac than through the wall of the normally pregnant uterus. In other cases the palpation is unexpectedly difficult, and in reviewing our cases we were impressed by the number in which this was so. Special note was made of the difficulty of palpating foetal parts in 6 of the 10 cases. In three the parts were felt with unusual ease. The remaining case (No. 1) was that of a patient with a pregnancy of 22 weeks. Little could be felt on abdominal palpation, but on vaginal examination the sac containing moving foetal parts could be felt easily through the posterior vaginal fornix. We concluded, therefore, that foetal parts may not be easy to feel in an extrauterine pregnancy, and that it is unwise to rely upon this sign to establish a diagnosis.

Unusual Attitude of Foetus.—The presence of an otherwise unexplained transverse or oblique lie should always arouse suspicion of an extrauterine pregnancy. This sign was found in five of our cases, but in the other five (including the 22-week pregnancy already referred to) the lie of the foetus could not be determined. The sign is not therefore constant or particularly reliable.

Absence of Uterine Contractions.—We do not think that it is possible to be sure that Braxton Hicks contractions are really absent unless the uterus has been palpated continuously for half an hour. This finding was of help in reaching a diagnosis in five of our cases. In the other five the diagnosis was made otherwise, and absence of contractions was not specially noted. The use of oxytocin to provoke contractions in cases of intrauterine pregnancy with a suspiciously lax uterus has been advocated by several writers, including Zuspan *et al.* (1957) We did not employ it in these cases of extrauterine pregnancy, but we were misled by it in the case, recorded later in this paper, of a normal intrauterine pregnancy erroneously diagnosed as being extrauterine.

Palpation of Empty Uterus on Bimanual Examination.—The most important single piece of information to be gained from pelvic examination is the palpation of the uterus apart from the gestation sac. This finding was present in 6 of our 10 patients. In one of the others who had a tubo-ovarian abscess a thorough examination was impossible because of tenderness. Foetal small parts were felt on vaginal examination in four cases—twice through the posterior fornix and twice through the anterior. This finding cannot be considered diagnostic of extrauterine pregnancy unless the empty uterus can be felt without doubt.

State of the Cervix.—Many authors have said there is an appreciable difference between the feel of the cervix in intrauterine and extrauterine pregnancies. Ware (1948) describes the cervix in extrauterine pregnancy as "long, thick, and firm," and says he has seen no case in which "the cervix was soft as it is in an intrauterine pregnancy at term." We do not agree with this.

TABLE I

Case	Age	Previous Obstetrical History	Gestation in Weeks	Site of Placenta	Management	Child				Convalescence
						On Admission	At Birth	Weight (g.)	Subsequent Progress	
1	35	2+1	22	In right broad ligament extending behind caecum and appendix	Total hysterectomy, right salpingo-oophorectomy; appendicectomy	A	SB	—	—	Uneventful
2	39	0+0	28	Behind left broad ligament extending into pouch of Douglas	Subtotal hysterectomy, bilateral salpingo-oophorectomy	D	SB	—	—	,,
3	33	0+0	33	In right broad ligament extending on to uterine fundus	Subtotal hysterectomy, right salpingo-oophorectomy	A	A	1,714	Died at 12 hours	,,
4	28	0+1*	35	In left broad ligament extending on to fundus and sigmoid	Subtotal hysterectomy, left salpingo-oophorectomy	A	A	2,170	Survived	,,
5	34	0+0	36	Left tube and back of left broad ligament	Left salpingo-oophorectomy	A	A	2,126	Survived (mildly spastic)	Mild urinary infection
6	29	2+1*	38	Anterior surface of right broad ligament	Right salpingo-oophorectomy	A	A	2,664	Survived	Mild ileus
7	30	1+0	40	In left broad ligament	Subtotal hysterectomy, left salpingo-oophorectomy	A	A	2,863	,,	Uneventful
8	35	2+1	43	Fundus and right broad ligament	Subtotal hysterectomy, bilateral salpingo-oophorectomy	D	SB	3,231	—	,,
9	24	0+0	46	Posterior surface of uterus and right broad ligament	Right salpingo-oophorectomy	D	SB	2,126	—	,,
10	27	0+1*	51	In right broad ligament	Placenta shelled out of broad ligament	D	SB	N.R.	—	,,

* Ectopic

In all our cases diagnosed before term the state of the cervix was regarded as normal for the duration of pregnancy, and in one (Case 6) the cervix was so soft and boggy that in the absence of an easily felt foetal presenting part the diagnosis of placenta praevia was, for a time, considered. On the other hand, in the two patients whose pregnancies had progressed beyond 44 weeks the cervix appeared to be reverting to its state before pregnancy and was found to be comparatively firm.

Constant Maternal Vascular Souffle.—We think this sign is of great value, and it does not appear to have been described before. The abnormally situated placenta often draws its main blood supply from the ovarian vessels on one or the other side, or (as in Case 6) from very hypertrophied vessels in the round ligament. If the ovarian vessels are dilated and hypertrophied a constant souffle can be heard just medial to the iliac spine on the side on which the placenta is located. In the case where the souffle appeared to arise from vessels along the round ligament the souffle was heard just above the inguinal ligament. This sign seems to be very useful, not only in contributing to the evidence needed to arrive at a diagnosis but also in providing a forewarning of where the placental site may be found, and which vessels may have to be ligated in order to control haemorrhage. This sign was noted in our early cases, and has been searched for in 9 of the 10. It was not looked for in Case 7, which was our first case. Of the other five patients with living foetuses, the sign was found in four (in Cases 1, 3, and 4 over the ovarian vessels, and in Case 6 over the round ligament), and was absent only in Case 5. No souffle has been heard in the four patients first seen after the death of the foetus. It seems reasonable to suppose that the maternal blood flow to the abnormally situated placenta diminishes after the foetus dies. Browne (1954) has demonstrated that the flow of maternal blood to the normal placenta virtually stops after intrauterine death of the foetus, but the mechanism by which this occurs is not understood. We are as yet unable to say how soon after death of the extrauterine foetus the souffle disappears. This souffle, when present, is distinctly louder than a normal uterine souffle, and is audible only over a quite small but constant area of the abdomen, as would be expected, since it usually originates in a single vessel, often the ovarian.

TABLE II

Case No.	Transverse Lie	Foetal Parts Behind Lumbar Spine	Gas Shadows over Foetus	Immobility	Lack of Uterine Outline	Other
3	+ Limbs caudad	−	+	Single set of *x*-ray films	+	
4	+ Limbs cephalad	+	+	+	+	Odd attitude
5	−	−	+	Single set of *x*-ray films	+	Feet in pelvis
6	—	−	+	−	−	
7	+ Limbs caudad	−	+	Single set of *x*-ray films	+	Feet in pelvis
8	,,	−	+	,,	−	Odd attitude. No Spalding
9	,,	No lateral film	−	,,	−	Feet in pelvis. Spalding present
10	+ Limbs cephalad	+	+	+	+	One hand in pelvis. Spalding present

Radiological Evidence

Various "pathognomonic" *x*-ray findings have been described as characteristic of extrauterine pregnancy. No one of these appears to be constantly present or invariably reliable as an aid to diagnosis. In our series radiographs were not taken in Case 2, and in Case 1 they merely confirmed the presence of a 22-week foetus. The findings in the other eight patients are summarized in Table II.

Position of Foetus.—Transverse lie is common, and was found in six of the eight cases. Snow (1952) is quoted by Yahia and Montgomery as saying that the foetus lying transversely inside the uterus usually lies back-downwards with its extremities directed cephalad, but that the extrauterine foetus commonly lies back-uppermost with the extremities directed down toward the maternal pelvis. In four of our cases the foetus was indeed back-uppermost, but in two it was back-downward (Fig. 1), suggesting that there may be exceptions to Snow's rule. In any case, a transverse lie with the back uppermost is not uncommon in cases of placenta praevia.

Attitude of Foetus.—This can best be described as exceedingly odd, though there is no characteristic attitude, as each foetus has to adapt itself as best it can to the space available for it. In some the spine is hyperextended, in others flexed, but almost invariably the head and/or the limbs are at unusual angles to the trunk (Fig. 1). A limb stretched down into the maternal pelvis is especially significant. In three cases a leg and in one case an arm were in this position, and in one of these (Case 7) a hysterogram showed that the foot actually lay below the level of the cervix (Fig. 2).

The appearance of foetal parts overlapping the maternal spine in a lateral view, as described by Weinberg and Sherwin (1956), seems to be a quite reliable indication of extrauterine pregnancy, when present (Fig. 3). We have never seen this in an intrauterine pregnancy. However, this sign was present in only two of our cases, so its absence does not exclude extrauterine pregnancy.

The presence of *gas shadows* over the foetus, or in lateral views anterior to it, seems to us suggestive but not conclusive of extrauterine pregnancy (Fig. 1). We have seen these with an intrauterine pregnancy.

The extrauterine foetus may remain in a singularly constant position and attitude in repeated radiographs.

FIG. 1.—A.-P. radiograph of extrauterine pregnancy at 30 weeks (Case 4). This shows the odd foetal attitude and the presence of gas shadows over the upper chest of the foetus. The back is downward—an exception to Snow's rule.

Films were repeated in only three of our cases. In Case 4 the position was constant and the foetus alive; in Case 10 the position was constant but the foetus dead; and in Case 6, with a living foetus, there had been a marked change of position between the two sets of films. The ability of the foetus to move seems to depend on the location of the gestation sac and the amount of liquor amnii.

In three of these cases a soft-tissue shadow was seen which could easily be mistaken for the outline of a normal pregnant uterus. It is hard to say what causes this appearance; possibly in some cases the gestation sac becomes thickened and probably also develops adhesions to omentum. The presence of a "uterine shadow" therefore does not exclude extrauterine pregnancy.

It seems, therefore, that the possibility of extrauterine pregnancy cannot be ruled out even if some or all of the so-called "characteristic" radiological signs of this condition are absent. Many of these signs can be found in cases of intrauterine pregnancy; indeed, the only sign which we think may be conclusive proof of extrauterine pregnancy is overlapping of the maternal spine by foetal parts in a lateral film.

FIG. 2.—Hysterogram showing empty uterine cavity (Case 7). The position of the cervix is shown by the cannula. Foetal feet (arrow) are seen below the level of the cervix.

FIG. 3.—Showing foetal parts overlapping the maternal spine. (Lateral view.)

We consider hysterograms to be contraindicated unless the diagnosis of extrauterine pregnancy has already been established beyond doubt, in which case they are of course redundant. We have taken hysterograms in three cases, but solely for teaching purposes.

A short summary of each of the 10 cases follows, to indicate the problems they presented in diagnosis and management.

Case 1

This patient, with active pulmonary tuberculosis, was referred with a diagnosis of menorrhagia due to fibroids. The last normal menstrual period had been 20 weeks previously; but there had been a two-week episode of lower abdominal pain and vaginal bleeding from the 13th to 15th weeks of pregnancy. The true diagnosis was suggested by palpation of a cystic mass behind the uterus and by hearing a constant souffle over the right ovarian vessels, and was confirmed by detecting foetal movement within the sac on vaginal examination.

At laparotomy the gestation sac was found to be within the right broad ligament, burrowing out to the pelvic sidewall, and adherent to caecum and appendix. It derived its blood-supply from the right ovarian and uterine vessels. It was dissected away from the structures on the wall of the pelvis and removed together with the uterus. The left tube and ovary were conserved. Convalescence was uneventful. The foetus was non-viable.

Case 2

This primigravida was uncertain of the date of her last menstrual period, but was admitted to hospital when approximately 28 weeks pregnant. There had been lower abdominal pain since the fourth month of pregnancy and foetal movement had ceased in the sixth month. She was febrile (103.6° F.—39.8° C.) and very ill. An abdominal mass present was thought to be the pregnant uterus, but no foetal parts could be felt and the foetal heart was not heard. There was marked tenderness and rebound tenderness in the right iliac fossa. Laparotomy was undertaken on a tentative diagnosis of either appendiceal or tubo-ovarian abscess together with a dead 28-week intrauterine pregnancy.

The gestation sac was on the left side, the placenta being attached to the back of the broad ligament and the side wall and floor of the pouch of Douglas. A large tubo-ovarian abscess was present on the right side. The dead foetus was removed after opening the sac; the uterus was removed together with both adnexa, including the placenta and the abscess. Despite this very major procedure her convalescence was uneventful.

This was the only one of our cases in which the diagnosis of extrauterine pregnancy was not made pre-operatively.

Case 3

This primigravida was seen first at the 30th week of pregnancy. She had no complaints. The uterus was thought to be big for the dates, and hydramnios was suggested. *X*-ray examination showed a transverse lie of the foetus, back uppermost, and the report stated: "The uterus is large relative to foetal development, consistent with a myoma below the foetus." She was admitted in the 33rd week because of anaemia and a persistent transverse lie.

Two days after admission she complained of slight epigastric pain and slight vaginal bleeding. Foetal parts could easily be felt above the umbilicus; the lie was transverse, with the head on the left. A vague soft mass could be felt above the pubes that later turned out to be the placenta. A loud souffle was heard over the right infundibulo-pelvic ligament. On vaginal examination the cervix was long and soft and the body of the uterus could be felt retroverted and displaced to the left, with a vague cystic mass on the right side of the pelvis. Fifteen minutes after the examination the patient said the pain had gone, but she felt that "the baby

had moved to the left side." No change in position could be detected on re-examination, but laparotomy was undertaken at once.

Liquor amnii was found in the peritoneal cavity, and a foot protruded through a rent in the amniotic sac. This was enlarged and the foetus was delivered. The placenta was in the right broad ligament, its maternal surface partly attached to the body of the uterus but in large part covered only by peritoneum. A haematoma developed quickly behind the placenta which rose upward in the abdomen, and the patient's blood-pressure dropped alarmingly. The membranes were opened beside the placenta and blood gushed forth; exploration under the placenta revealed only a few fine stringy adhesions. The bleeding subsided somewhat when the right ovarian vessels were clamped, and was finally controlled by removal of the body of the uterus together with the placenta. The baby weighed 3 lb. 12¼ oz. (1,714 g.) but died after 12 hours; post-mortem examination showed atelectasis. The mother's convalescence was uneventful.

Reference is made below to the problem of retroplacental bleeding in pregnancies within the broad ligament. It seems as though only the intra-abdominal and intra-amniotic pressure enable the placenta to retain its tenuous hold on the thin peritoneal covering over its maternal surface, and when the sac is opened and the foetus is removed nothing will then prevent massive retroplacental bleeding.

Case 4

This patient was first seen at the 30th week of pregnancy. Seven weeks before her last menstrual period she had been admitted to another hospital with an ectopic pregnancy, and left salpingo-oophorectomy and appendicectomy had been done. The present pregnancy had been symptomless except for constipation.

The foetus lay transversely, high in the abdomen with the head under the right costal margin. A definite souffle was heard over the left infundibulo-pelvic ligament (which was puzzling, as we thought the pregnancy must have arisen from her remaining *right* tube and ovary). On vaginal examination the uterus was felt, retroverted and pushed down into the pelvis by the gestation sac. *X*-ray films (Fig. 1) confirmed the foetal position and the presence of a soft-tissue mass below it. Since this seemed to be the patient's last chance to have a child, she was kept under observation in hospital until the baby became more mature. Repeat *x*-ray examination a month later showed the position and attitude of the foetus to be quite unchanged.

By the end of the 35th week everyone, including the patient, had become very apprehensive about waiting longer for this "obstetrical time-bomb," and the baby seemed to have grown. At laparotomy, many omental adhesions to the sac were divided, the sac was opened, and the living foetus was delivered. The sac appeared to be within the left broad ligament. The placenta was partly attached to the body of the uterus and partly covered only by peritoneum. Massive bleeding occurred from the latter area; the patient's blood-pressure dropped, but rose again after the left ovarian vessels had been identified and clamped. The sac was freed from small bowel, pelvic colon, and bladder peritoneum; the leaves of the broad ligament were divided close to the side wall of the pelvis, and the body of the uterus was removed with the placenta. The right tube and ovary were grossly normal and were conserved. Six pints (3,400 ml.) of blood was transfused during the operation.

Convalescence was uneventful. The child weighed 4 lb. 12¼ oz. (2,170 g.) and progressed well. Lactation was normal.

Case 5

This primigravida was uncertain of her dates, but was probably 30 to 32 weeks pregnant when first seen at the antenatal clinic. She then complained of vague lower abdominal pain during the previous month. One month later she returned, having had more severe abdominal pain for three days, and was admitted with a provisional diagnosis of a degenerating myoma. Foetal parts were hard to feel. No souffle was heard. *X*-ray examination showed the foetus in the right side of the abdomen presenting as a breech, with the feet hanging into the pelvis. Limbs could be felt easily through the anterior fornix.

At laparotomy the living foetus was found lying free in the peritoneal cavity, which also contained liquor amnii and old blood-clot. The placenta was attached to the region of the left tube and the back of the left broad ligament. The ovary was not found. Severe retroplacental bleeding occurred, but the infundibulo-pelvic and round ligaments were clamped and the placenta could then be removed. The uterus was conserved together with the right adnexa.

The mother's convalescence was uneventful save for a mild urinary infection. The baby weighed 4 lb. 11 oz. (2,126 g.) and made good progress. Lactation was adequate.

The baby was brought back to the hospital at the age of 18 months and was then found to be mildly spastic.

Case 6

This patient had had two normal pregnancies. Two months before her last period a left salpingectomy was done for a tubal ectopic pregnacy. She attended the antenatal clinic regularly from the 27th week of pregnancy onward. At 31 weeks she complained of slight lower abdominal pain, and a little tenderness was found in the left lower quadrant. At 35 weeks the foetus was noted to be difficult to palpate but lying transversely and high in the abdomen. This position was confirmed by *x*-ray examination. At 36 weeks the pain grew worse and the abdomen was more distended, suggesting the diagnosis of hydramnios. The position of the foetus was observed to change. A loud souffle was heard over the right inguinal ligament. No Braxton Hicks contractions could be felt. Examination under anaesthesia confirmed that the uterus could be felt below the gestation sac. A sound passed for 4 in. (10 cm.) into its cavity. Immediate laparotomy was performed.

The sac was opened and a living foetus was delivered. The placenta was attached mainly to the anterior surface of the right broad ligament, securing its blood supply from the right ovarian vessels and grossly hypertrophied vessels in the round ligament. When the placenta was lifted out of the wound these formed an immensely vascular pedicle, which was compressed digitally to control bleeding until the vessels could be identified and clamped. The right tube and ovary could not be identified and were presumably removed with the placenta. The left adnexa were absent. On cleaning out the peritoneal cavity a few small old blood-clots were found, so presumably there had been earlier bleeding from the placental site, which may have explained the recent pain.

The mother's convalescence was complicated by mild ileus. The child, a female, weighed 5 lb. 14 oz. (2,664 g.) and it thrived.

Case 7

This patient, the first in our experience, had had a normal pregnancy and delivery seven years previously. She was first seen at the antenatal clinic when she was one day past term. A round firm mass, the foetal head, could be seen and felt just under the abdominal wall above the umbilicus; as she lay on the table it rose above the pregnant abdomen like the dome of St. Paul's Cathedral. The pregnancy had been uneventful. *X*-ray films were taken, confirming the position of the foetal head and showing that a leg stretched low into the pelvis. While the films were being processed the patient disappeared from the clinic.

She returned the next morning to the labour ward in spurious labour. As this was our first case we did not seek a souffle, and no pelvic examination was made, though a hysterogram (Fig. 2) was done before the patient was taken to the operating theatre.

At laparotomy the gestation sac was found to be in the left broad ligament, displacing the uterus forward and to the right. The foetus and meconium-stained liquor could be seen clearly through the membranes. The sac was very mobile and was brought out of the abdomen before it was opened. After the child was delivered the placenta was

found to be within the left broad ligament, with only a few adhesions to the appendices epiploicae of the sigmoid. In this case no retroplacental haemorrhage occurred, but the placenta was nevertheless removed together with the body of the uterus. It seemed to have gained its principal blood-supply from the ovarian vessels.

The mother's convalescence was satisfactory. The child was distorted at birth from the position it had been forced to adopt during growth, but it survived and developed normally. The birth weight was 6 lb. 5 oz. (2,863 g.).

On examination of the specimen the uterine end of the tube could be seen blending with the placental mass. Serial sectioning showed no trace of ovarian tissue. It was presumed that the pregnancy had been primarily tubal, and had ruptured between the layers of the mesosalpinx early in pregnancy and had continued to develop there.

Case 8

This patient gave a history of two previous full-term pregnancies and one abortion. She attended the antenatal clinic from the 19th week of this pregnancy and had passed as normal until the 38th week, after which she defaulted from the clinic. She was admitted with a history of vague abdominal pains at the 43rd week of pregnancy.

The head could be felt just under the abdominal wall, and *x*-ray examination showed a transverse lie with a curious foetal attitude. The foetal heart was silent and no movement was felt. No souffle was heard. The cervix was long and soft, and the uterus could be felt below the gestation sac, anteverted and in the midline.

At laparotomy the intact sac was found to be adherent to omentum and sigmoid. The placenta was attached to the fundus of the uterus. The sac was opened, and after the infant had been delivered the placenta bled very freely. The exact relations were difficult to establish, and in order to control bleeding both infundibulo-pelvic ligaments were clamped. Subtotal hysterectomy and bilateral salpingo-oophorectomy was done. As it turned out, the placenta was more on the right side, and the normal left ovary could have been conserved if its blood-supply had not already been cut off. The absence of a souffle might have suggested that the blood-flow to the placenta had been reduced after the death of the foetus, but at operation this did not appear so. This was the only case in our series with a still-born baby in which the placental haemorrhage was serious.

The mother's convalescence was uneventful. The stillborn baby weighed 7 lb. 2 oz. (3,231 g.). It showed no maceration, and death was presumed to have been recent. Post-mortem examination showed evidence of anoxia.

Case 9

This primigravida was first referred to hospital when the pregnancy had continued to 46 weeks. At the 25th week there had been a four-day episode of abdominal pain, vomiting, and diarrhoea, but no vaginal bleeding. A similar episode accompanied by bleeding "like a normal menstrual period" occurred at the 36th week. After this, foetal movement ceased and there was regression of abdominal and breast enlargement. A further "menstrual period" had occurred during the 45th week of pregnancy.

An abdominal mass reached to the level of the umbilicus. Foetal parts could not be felt, the foetal heart was not heard, and no souffle was detected. The uterus could be distinguished lying in anteversion below the sac, and foetal parts were felt through the posterior fornix. A hysterogram was done, and foetal limbs could be seen in the pelvis.

At laparotomy the uterus was displaced upward and forward by the gestation sac, which occupied the pouch of Douglas and was densely adherent to the right broad ligament and the right pelvic wall. The sac was opened and the foetus removed. The right adnexa and the adherent placenta were removed. The membrane adherent in the pouch of Douglas was left *in situ*. There was very little bleeding. The placenta seemed to have been supplied mainly by the right ovarian vessels.

Convalescence was normal. The grossly macerated foetus weighed 4 lb. 11 oz. (2,126 g.). The placenta showed degenerative changes, including dystrophic calcification.

Case 10

This patient gave a history of salpingectomy for a right tubal pregnancy in 1955, two years previously. She had attended the antenatal clinic at a country hospital and had remained well until the 34th week of pregnancy, when she began to have mild constant left-sided abdominal pain. Foetal movements ceased at the 37th week, and the pain disappeared a week later. The size of the abdomen then became less. In the 48th week of pregnancy there was dark vaginal bleeding for six days. Attempts at induction failed, and the patient was referred to this hospital a week later. The diagnosis of extrauterine pregnancy was not made, and after further unsuccessful attempts at medical induction of labour the patient was sent home to await spontaneous labour.

She returned in the 51st week of pregnancy, having had further vaginal bleeding for three days with intermittent abdominal pain. The foetus could now be felt more easily. No souffle was heard. The cervix was firm and the uterus could be felt distinctly. *X*-ray examination showed a macerated foetus with one arm reaching into the pelvis, and foetal parts overlapping the maternal spine (Fig. 3).

When the abdomen was opened the placenta was found to be in the right broad ligament, displacing the uterus to the left and downward. The left tube and ovary were adherent to the pelvic wall and the sigmoid. The macerated foetus was in the peritoneal cavity; omentum adhered to its head and small bowel to its legs and body. One arm was in the pelvis behind the placenta, and the cord ran across the utero-vesical pouch, lightly adherent to peritoneum. The adhesions were easily separated and the foetus was removed. The placenta was not at all vascular. The round ligament was divided, the anterior leaf of the broad ligament was opened, and the placenta was literally shelled out of the broad ligament without bleeding, even where it had extended to the lateral pelvic wall and up behind the caecum. The right infundibulo-pelvic ligament was ligated.

Convalescence was smooth. Unfortunately, the macerated foetus was not weighed. The placenta was avascular and meaty. The suspensory ligament of the ovary could be identified running into it, but no ovarian tissue was found.

An Incorrect Diagnosis

The accounts of these cases indicate that advanced extrauterine pregnancies may present with a wide variety of symptoms and signs. As our experience has grown, we have developed the "high index of suspicion" advocated by Cross *et al.* (1951) as the most important attribute leading to successful diagnosis of this condition. But the diagnostic signs are fallible, and the high index of suspicion may occasionally lead to an error in diagnosis, as shown by the following case.

Case 11

A woman aged 26 had previously had three normal deliveries and an appendicectomy. She first attended the clinic at the 23rd week of her fourth pregnancy. There had been no pain or bleeding. The abdomen was thought to be a little large for this duration of pregnancy. A small foetus was very easily felt, lying transversely. A souffle was heard in the left iliac fossa, quite constant but not quite so loud as in the cases described previously. The cervix was long and firm, and it was thought that a rather small uterus could be felt below the gestation sac. She was admitted for investigation. No Braxton Hicks contractions could be felt, and no contractions were produced by an intravenous "pitocin" drip (10 units in 500 ml.) at a rate gradually increased to 4 ml. a minute. *X*-ray examination showed the foetus lying transversely, back uppermost, with the limbs stretched down

towards the pelvis. No uterine outline could be seen and there were numerous gas shadows overlying the foetus.

Examination under anaesthesia confirmed the impression of a small uterus below and probably attached to the gestation sac.

The abdomen was opened, and an apparently normal *intra*-uterine pregnancy was found. The foetus occupied the rather lax upper segment, and the lower segment was firm and unexpanded. The abdomen was closed and the pregnancy progressed uneventfully to term.

This has been a salutary experience, but were we now confronted by a similar case we would be strongly inclined to act in the same way, though perhaps we would observe the patient rather longer before deciding upon a laparotomy.

Management

When Should we Operate?

Most authorities advise laparotomy as soon as the diagnosis is made. Beck (1919) thought the optimal time for intervention was between the sixth and seventh months of pregnancy, and we consider that the diagnosis will seldom be made earlier than that. But what if the foetus is alive? Beck thought there was little additional risk in delaying operation until the 38th week in the hope of obtaining a live child. Others believe the risks of such delay to be "unpredictable and grave" (Hibbard, 1957), and point out that foetal abnormalities are common—30 to 50% according to Zuspan *et al.* (1957). They therefore conclude that the interests of the baby should be disregarded. Our series, which contained no foetal abnormalities, leads us to agree with Mahfouz (1938) that this possibility should not influence one's decision. When the foetus is alive it seems reasonable to assume that haemorrhage may be more serious near term than in the middle trimester of pregnancy, but we think that the risk of haemorrhage depends more on the location of the placenta than upon its maturity. The decision to delay operation for five weeks in Case 4 resulted in a happy outcome, which more than compensated for the anxious period of waiting.

Our conclusion is that operation may be delayed in some cases until the foetus attains a reasonable size. The patient must remain in hospital. Blood must be kept available for immediate use. Pain may indicate intraperitoneal rupture of the membranes (Cases 3 and 5) or haemorrhage (Case 6), and necessitates immediate operation.

The situation is quite different when the foetus is dead. We know of no way to determine when the placental site has lost its excessive vascularity. Serious bleeding occurred in Case 8, with a foetus quite recently dead, but there was no difficulty in Cases 9 and 10, in which the foetus had been dead for 10 and 14 weeks respectively. These patients came to no harm during the long interval after intra-abdominal death of the foetus, and we suggest that when the foetus has died it may in fact be the safest procedure to wait for six to eight weeks before opening the abdomen, provided no evidence of infection develops meanwhile. It may not be necessary to wait so long. McClure Browne (1959, personal communication) considers that the placental circulation is much reduced within 48 hours after intrauterine death of the foetus, and the same may prove to be true of an extrauterine placenta.

Can we Predict the Site of the Placenta?

In some cases we think that the discovery of a souffle may help to determine on which side of the pelvis the placenta is situated and which vessels provide its main blood-supply. The importance of this was impressed upon us by those cases (Nos. 3, 4, 6, and 8) in which rapid clamping of the ovarian vessels controlled alarming haemorrhage. Pelvic examination under anaesthesia before laparotomy may also help to establish the placental site. We do not think that ordinary *x*-ray techniques are of much help in locating the placenta, and aortography seems to us much too difficult and dangerous a procedure to employ in these patients.

What Should be Done with the Placenta?

There is no easy answer to this question. We have been fortunate so far, since in our cases it has been possible to remove the placenta either alone or together with its site of attachment. This seems to be the best thing to do when it is possible, though it necessitated hysterectomy in six of our patients. The fact that five of these were subtotal is an indication of the severity of the bleeding that occurred. Undoubtedly there are cases where removal is impossible, and if there is no bleeding behind the placenta it should then be left strictly alone.

We have, however, been most impressed by the rapidity and volume of retroplacental bleeding in some of our cases. This is particularly serious when the placenta has developed between the layers of the broad ligament. Here all or part of the maternal surface of the placenta is covered only by a thin sheet of peritoneum, and after it has been removed the cotyledons can be seen clearly through the covering membrane. Its attachments are most tenuous, and one wonders why it has not become detached from its site early in pregnancy. Histological studies (see below) suggest that the pool of maternal blood is kept from spreading beyond the edge of the placenta by massive deposits of fibrin. Apart from this fibrin ring around the edge of the placenta, the only factor preventing placental separation seems to be the pressure inside the amniotic sac. When this is released by opening the abdomen and the membranes and removing the foetus, an immediate retroplacental haematoma forms, as was observed in Cases 3, 4, 5, 6, and 8. We cannot explain why this did not happen in Case 7. However, it would obviously be most dangerous to leave such a loosely attached placenta *in situ*.

The only direct reference to this problem that we have been able to find in the literature is the account by Stromme *et al.* (1959) of a case in which development of a haematoma behind part of a placenta attached to the broad ligament compelled them to remove part of the placenta instead of leaving it all *in situ* as they had planned. Care should be taken to open the sac well away from the edge of the placenta in case the latter proves to be firmly attached to some structure which cannot be removed.

Attachment of the Placenta

All the placentae were examined carefully. Three main characteristics were evident on macroscopic examination. (1) The anatomy was greatly distorted. In some cases part of the fallopian tube could be seen leading toward the placental mass. In no case was ovarian tissue identified either macroscopically or in histological sections. (2) There was tremendous hypertrophy of all vessels near the placenta. (3) The placenta itself appeared relatively healthy, and normal in size and shape for the stage of pregnancy.

Numerous sections were studied to try to determine how the extrauterine placenta is attached. Areas of placenta attached to relatively firm structures, such as the fundus of the uterus (Fig. 4), show amazingly little trophoblastic invasion as compared with a normal intrauterine placenta (Fig. 5). The reason for this difference is obscure. Possibly trophoblastic invasion and the development of strong "anchoring villi" depend partly on the presence of a true decidua, and in the absence of this is handicapped. It makes one wonder whether the extrauterine placenta is ever so firmly attached to its site of implantation that it can safely be left to absorb.

Placenta covered only by a layer of peritoneum shows no anchoring villi at all (Fig. 6), and in this case the mechanism by which the maternal blood is kept in the space behind the placenta (in this circumstance a "chorio-peritoneal" rather than chorio-decidual space) is a matter for speculation, as also are the dynamics of the circulation within the space. If, as we have suggested, the placenta is held against its site of attachment by intra-abdominal and intra-amniotic pressure, it follows that this pressure and the pressure of the blood within the space must be very nearly the same; otherwise either the placenta would be forced off its bed or the blood would be prevented from entering the space. How this precarious balance is maintained despite changes produced by straining or by hypertension must be a matter for conjecture.

The extrauterine placenta seems to have a thick ring of fibrin around its margin (Fig. 7), in marked contrast to the normally situated placenta (Fig. 8). Presumably it is this ring which prevents the retroplacental pool of blood from leaking out under the placental margin. How it develops, and how reliable it is as a safeguard against sudden and possibly fatal haemorrhage, are problems which need much more study, but it is noteworthy that Playfair (1893) referred to the exudation of a "plastic material" around the gestation sac caused by the irritation of the ovum.

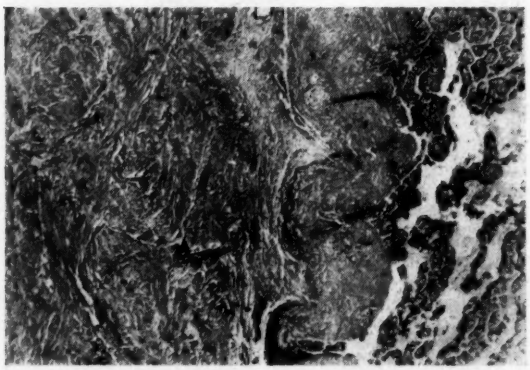

FIG. 4.—Areas of placenta attached to fundus of uterus.

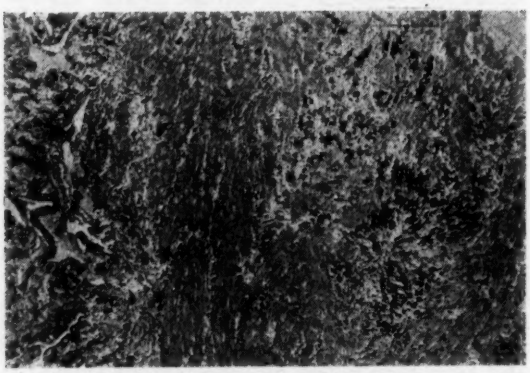

FIG. 5.—Normal uterine placental site.

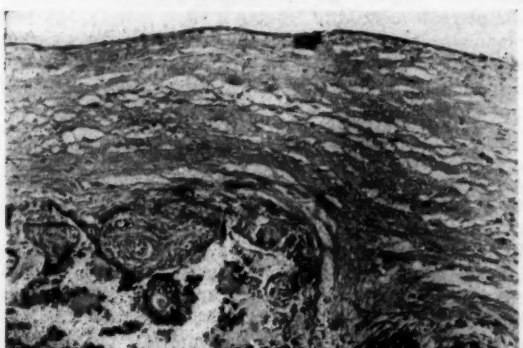

FIG. 6.—Placenta covered only by layer of peritoneum, without anchoring villi.

Summary

Ten cases of advanced extrauterine pregnancy are described. All the mothers and four babies survived.

The difficulties of diagnosis are discussed and are illustrated by the report of an additional case which had many of the characteristics of extrauterine pregnancy but which proved to be normal and intrauterine.

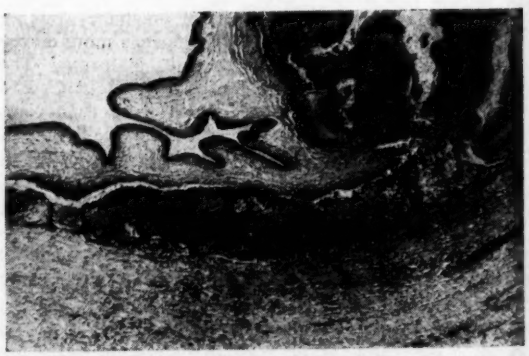

FIG. 7.—Extrauterine placenta apparently with a thick ring of fibrin around its margin, in marked contrast to the normally situated placenta.

FIG. 8.—The edge of a normally situated placenta.

Attention is directed to the frequent presence of a loud souffle heard over the small area of abdominal wall overlying the hypertrophied vessels supplying the placenta.

While most cases should be dealt with by immediate laparotomy, it may be justifiable on some occasions and with adequate safeguards to allow the pregnancy to continue until the foetus is certainly viable. When the foetus has just died it may be safer to defer operation until the placenta has became avascular.

It is suggested that, whenever possible, the placenta should be removed together with the structures to which it is attached. The special case of the placenta situated within the broad ligament is described. Severe retroplacental bleeding seems inevitable in such circumstances.

A preliminary report of histological studies of the implantation of the extrauterine placenta is included. The problem of how the placenta maintains its precarious attachment until late pregnancy is raised but not solved.

Our thanks are due to our colleagues past and present, notably Professor J. H. M. Pinkerton and Dr. G. T. M. Cummins, who have shared with us the tribulations and rewards of these cases. We are especially indebted to Dr. W. B. Robertson for his invaluable help and advice on the histology.

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"In the years during which I was surgeon to the Albert Dock Hospital (1919 to 1956), I saw many changes in the Health Faculty of my patients. An observer, if he could see and compare the out-patient department of fifty years ago with that of to-day would, I think, be struck first by the revolution in personal cleanliness. In my young days the patient had to be scrubbed before being admitted to bed in the general ward. Their bodies were not just soiled with the dust and sweat of the day's work, but were ingrained with the grime of weeks of neglect. Women, if anything, were worse than men with their greasy straggly rat-tails of hair covered with equally greasy cloth caps. No woman was admitted until her head had been deloused. All patients were verminous." (*The Health of the Dock Worker*, Sir Hugh Griffiths. National Dock Labour Board, Education Booklet No. 2.)

CLINICAL ANALYSIS OF 100 CASES OF SEVERE MEGALOBLASTIC ANAEMIA OF PREGNANCY

BY

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The purpose of this paper is to report on the medical and obstetrical aspects of 100 cases of severe megaloblastic anaemia of pregnancy which have been diagnosed in a six-year period (1953 to 1958 inclusive) at the Rotunda Hospital, Dublin. The findings are compared with those of several similar studies made recently in other centres. The importance of this condition as a cause of maternal and foetal complications is discussed.

Incidence and Degree of Anaemia

It is now realized that megaloblastic anaemia is a comparatively common complication of pregnancy. This series of 100 cases represents an incidence of 1 in 240 confinements (Table I). This figure is slightly lower than the true one because some cases which were delivered on the hospital district were not included owing to incomplete documentation. Higher incidences of this complication have been reported by other workers: Forshaw (1958) found an incidence of 1 in 67 hospital confinements, and Giles and Shuttleworth (1958) found a frequency of megaloblastic anaemia as high as 2.8% of hospital confinements. It seems that the marrow may become megaloblastic in pregnancy with a relatively high haemoglobin (Forshaw *et al.*, 1957), and therefore such patients may in fact be physically well and not in need of treatment. It is emphasized that all cases here reported were clinically anaemic or ill, and that each represented examples of the disease of moderate or severe degree. Each case was a practical problem requiring immediate treatment. Table II shows the degree of anaemia in these cases at the time of diagnosis.

TABLE I.—*Incidence of Megaloblastic Anaemia at Rotunda Hospital*

Year	No.	Year	No.
1953	15	1957	22
1954	13	1958	21
1955	12		
1956	17	Total	100

Incidence approximately 1 in 240 pregnancies. 23 cases occurred in primigravidae.

TABLE II.—*Degree of Anaemia When Diagnosed*

Hb (g.)	No.	Hb (g.)	No.
2·0–2·9	1	6·0–6·9	18
3·0–3·9	5	7·0–7·9	28
4·0–4·9	10	8·0–8·9	15
5·0–5·9	22	9·0–9·9	1

Seasonal Incidence.—In 1957 Thompson, reporting a series of 100 cases from Newcastle taken from the records of over twenty years, found an increased incidence of the disorder during the winter and spring months. He believed that this suggested that dietary deficiency was at least a contributory cause of this disorder. Forshaw (1957) found a similar seasonal incidence amongst his cases, but this was not found by

Giles and Shuttleworth (1958) nor by Mollin *et al.* (1959). In our series a convincing seasonal pattern was not shown.

Recognition and Diagnostic Criteria

Approximately 30% of these cases presented as patients with progressive anaemia of pregnancy which had failed to respond to oral or parenteral iron. In many other cases anaemia was not the presenting problem, and more prominent features were such symptoms as vomiting, diarrhoea, and pyrexia (Table III). Oedema and albuminuria at some stage were particularly common. This led to some of these cases being mistaken initially for toxaemia of pregnancy (see below). Vomiting, pyrexia, urinary infection, and diarrhoea were present in a smaller proportion of cases, particularly in the puerperium, and often led to delay in diagnosis.

TABLE III.—*Symptoms Other than Those of Anaemia* (100 *Cases*)

Oedema	51	Pyrexia	71
Albuminuria	44	Urinary infection	11
Hypertension	23	Diarrhoea	10
Vomiting	17		

Final diagnosis was established in all cases by the finding of megaloblasts in the bone marrow, or in the peripheral blood by examination of the buffy coat. In all these cases 20 mg. of folic acid daily caused a reticulocyte response and a rise in haemoglobin level.

TABLE IV.—*Associated Conditions*

Carcinoma stomach	1	Urinary infection	11
Hodgkin's	1	Epilepsy	3
Lymphadenopathy	1		

Associated Conditions (Table IV)

Megaloblastic anaemia may occasionally arise in pregnancy as a complication of some other disease. Carcinoma of the stomach presented in this way in one patient, and another patient with Hodgkin's disease developed megaloblastic anaemia. Urinary infection has already been mentioned, and the incidence in megaloblastic anaemia is undoubtedly higher than normal. Three out of 100 cases of megaloblastic anaemia were under treatment for epilepsy. This incidence is very much higher than the average incidence of epilepsy in the overall attendance at the hospital over the period under study, which was about 1 in 400. It has been shown in recent years that certain anticonvulsants can cause the development of megaloblastic anaemia (Badenoch, 1954; Berlyne *et al.*, 1955; Hawkins and Meynell, 1958). It seems likely that the administration of these drugs was a factor in the development of megaloblastic anaemia in these cases. This aspect is fully discussed in a separate publication (Gatenby, 1960).

Time of Diagnosis

In earlier papers on this subject diagnosis was made more often during the puerperium (Davidson *et al.*, 1942); Miller and Studdert, 1942). More recently, as the anaemia is being watched for more closely, nearly half these cases are being recognized antenatally. In this series 41 of 96 were diagnosed before delivery (Table V). Giles and Shuttleworth (1958) by intensive investigation managed to find 62 antenatal cases as against 28 in the puerperium. Chanarin *et al.* (1959) have summarized the findings in relation to time of diagnosis from 20 reports in literature. Their tabulation shows clearly that most of the cases recognized before delivery are diagnosed between 31 and 40 weeks' gestation. All our antenatal cases were found during this period, and most of these were during the last four weeks of pregnancy. The puerperal cases are usually recognized within the first fortnight (Table V) after delivery.

TABLE V.—*Time of Diagnosis*

	Pregnancy (41 Cases)										Puerperium (48 Cases)						
Weeks	30	31	32	33	34	35	36	37	38	39	1	2	3	4	5	6	7
Number	1	0	2	1	2	1	8	4	10	12	24	13	5	3	1	1	1

Obstetrical Aspects

Toxaemia.—The association of megaloblastic anaemia of pregnancy with toxaemia has been noted on many occasions (Davidson *et al.*, 1948; Scott and Govan, 1949; Giles and Shuttleworth, 1958; Tacchi, 1958). Difficulty may arise in differentiating the two conditions owing to the frequency of oedema and albuminuria in patients with megaloblastic anaemia. In this series oedema was noted in 51 cases and albuminuria in 44. Hypertension (B.P. of 140/90 or greater on one or more occasions) was noted in 23 patients. It is felt that whenever hypertension is present the cause must be regarded primarily as one of toxaemia, but when oedema and/or albuminuria occurs without hypertension these features may be due to, or directly associated with, the anaemia itself, and the case cannot be regarded as one of toxaemia. Thus in the present study hypertension alone occurred in 23% of cases, hypertension with oedema or albuminuria in 22%, and hypertension, oedema, and albuminuria in 14%. The hospital incidence of toxaemia over the same period was approximately 6%, thus, whichever criterion of toxaemia is accepted, it would appear that it is much more frequent in association with megaloblastic anaemia.

Parity.—There were 23 primigravidae in this group of 100 cases. In the remainder full-time parity varied from 2 to 16. The average figure for the whole group was 3.8.

Twins and Hydramnios.—An increased incidence of multiple pregnancy has been mentioned by several authors (Thompson, 1957; Giles and Shuttleworth, 1958; Tacchi, 1958; Chanarin *et al.*, 1959). This is borne out in the present series with an incidence of 8% (twins, 7; triplets, 1). An association with hydramnios has not been previously recorded. Hydramnios was noted in nine cases whereas the general hospital incidence is in the region of 1.2%. This high incidence cannot be explained by the frequency of multiple pregnancy as only two of these cases were multiple pregnancies (twins, 1; triplets, 1), and thus it was found in seven cases of single pregnancies. One of these was a case of hydrops foetalis, but there was no foetal abnormality in any of the remaining six.

Premature Labour.—Premature labour is said to be common in this group (Stevenson, 1938; Callender, 1944). Tacchi (1958) reported 18 out of 52 who were delivered before the 38th week. In the present series, 22 out of 80 known cases were delivered before the 38th week, an incidence of 27%. On the other hand, 23 infants from 17 pregnancies were premature by weight, that is, less than 5½ lb. (2.5 kg.). As these figures were taken from a total of 88 known cases the premature incidence was 19.3%. Excluding multiple pregnancies, the premature incidence in single pregnancies was 12.5%. The incidence of prematurity (by weight) in the hospital is approximately 8%, and therefore there is an increased incidence of premature labour and prematurity even when multiple pregnancy is excluded.

Haemorrhage.—Badenoch *et al.* (1955) reported two cases of post-partum haemorrhage out of nine cases under review and drew attention to this high incidence. In the present series there were two cases of P.P.H.—one traumatic following normal delivery and the other secondary. This incidence corresponds with the general incidence of P.P.H. in the hospital, which is approximately 2.2%. Considering the supposedly high incidence of toxaemia, accidental haemorrhage was not unduly common, and was seen on two occasions. There was one case of placenta praevia.

Duration of Labour.—In 8% of cases the duration of labour exceeded 24 hours, but in only one case did it exceed 48 hours. This is of little significance, as the hospital incidence of prolonged labour (greater than 48 hours) is approximately 1.7%. However, the general impression was that labour is usually short and the preponderance (increased incidence) of multiparity is probably a sufficient explanation.

Method of Delivery.—The only finding of any significance so far as method of delivery is concerned was a relatively lowered incidence of forceps delivery (10% against a general incidence of 13–16%). This again is probably explained by the increased multiparity.

Induction of Labour.—Induction of labour is generally better avoided in these cases. Occasionally, for some associated reason, it becomes necessary, and in this series 8% of cases were induced (five surgical inductions and three medical inductions). This corresponds with the general incidence, which for surgical induction is approximately 6–7%.

Stillbirths and Neonatal Deaths.—In the series there were three stillbirths, none of which could be ascribed to the anaemia, and the incidence corresponds with the hospital stillbirth rate of 2.9%. As would be expected, considering the high incidence of prematurity, the neonatal death rate was increased. There were six neonatal deaths—five due to prematurity and one to anencephaly. The hospital neonatal death rate is approximately 1.5%, and the high incidence of 6% is entirely explained by the frequency of premature labour, prematurity, and multiple pregnancy.

Pyrexia and Morbidity.—The association of pyrexia has been frequently noted (Dockeray, 1938; Ungley, 1938; Miller and Studdart, 1942; Callender, 1944). Pyrexia was found in 71% of cases and puerperal morbidity in 30%.

Maternal Mortality.—There were two deaths in the 100 cases, not from anaemia, but, from underlying malignant disease. One was a case of Hodgkin's disease and the other carcinoma of the stomach. Both cases presented with megaloblastic anaemia.

Recurrence of Megaloblastic Anaemia.—This was not common. Megaloblastic anaemia occurred in a second pregnancy in four cases in the six-year period.

Discussion

Megaloblastic anaemia promptly responds to folic acid, and Chanarin *et al.* (1959) have shown that there is clearly a folic acid deficiency of the tissues in this disease. Lack of sufficient folic acid in the diet to meet the demands of pregnancy could certainly cause anaemia, and this would explain the high incidence in multiple pregnancy. However, no clear relationship between inadequate diet and the incidence of this anaemia has yet been demonstrated in these islands. Impaired absorption of folic acid or interference with its metabolism may be important in many cases. Certainly this anaemia may occur in women, who apparently have had adequate nourishment before and during their pregnancies.

Over the last few years evidence has been gathered from many different centres in the British Isles that megaloblastic anaemia occurs as a complication in pregnancy much more frequently than was formerly thought. In our experience 1 in 240 pregnant women will have serious anaemia of this type, and milder degrees of the same condition must occur quite often. Apart from causing a period of serious ill-health in the mother, there is an increase in neonatal deaths due to the high rate of prematurity in this group. There is also an associated increase in the incidence of hydramnios and multiple pregnancy, which in turn may be partly responsible for the higher incidence of toxaemia.

The prevention of megaloblastic anaemia by the routine administration of folic acid in pregnancy would seem an obvious solution to this problem. Some have accepted this principle (Lowenstein *et al.*, 1955; Francis and Scott, 1959). The main disadvantage in the prophylactic use of folic acid therapy is that megaloblastic anaemia not caused purely by the demands of pregnancy will be masked and lead to delay in recognizing the underlying cause, which may be serious. Admittedly this is a small group, but malignant disease occurring in pregnancy may first manifest itself by megaloblastic anaemia (as in two of our cases). Again, there is always the possibility of an Addisonian anaemia being masked, and it is well known that folic acid may precipitate serious neurological changes; but this anaemia is very rare in pregnancy, and we have seen only one case since 1953. On the whole the argument in favour of routine antenatal administration of folic acid is very strong, and probably this procedure will be adopted more widely in the future. It is suggested, at any rate, that in all cases of multiple pregnancy supplementary folic acid should be given.

Summary

The incidence, clinical features, and obstetrical aspects of 100 cases of severe megaloblastic anaemia in pregnancy and the puerperium occurring over a six-year period (1953 to 1958 inclusive) at the Rotunda Hospital, Dublin, are recorded. The incidence has been 1 in 240 confinements, and is associated with an increase in the neonatal death rate (6%), largely due to prematurity.

The advisability of using folic acid as a routine prophylactic in pregnancy is discussed.

We wish to thank Dr. E. W. L. Thompson, ex-Master, and Dr. A. D. H. Browne, present Master of the Rotunda Hospital, for affording facilities and giving permission to publish. We also thank Dr. H. C. Moore, the pathologist, who was in charge of the haematology of all these cases, for his valuable assistance.

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MEGALOBLASTIC ERYTHROPOIESIS IN PREGNANCY

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During recent years a great deal of attention has been paid to the problem of anaemia in pregnancy. In the antenatal clinic of Sunderland Maternity Hospital, which caters for about 1,800 cases a year, 25% of mothers have at the 32nd week of pregnancy haemoglobin levels below 70%, which Whitby and Britton (1957) regard as the lower limit of normality. Undoubtedly most cases of anaemia in late pregnancy are due to iron deficiency, but there is a growing volume of opinion that many cases are anaemias of megaloblastic type.

As recently as 1951 Thompson and Ungley described 45 cases of megaloblastic anaemia of pregnancy collected over a period of 17 years, while Clark (1952) reported 18 cases in a 7½-year period, an incidence of one case in 1,708 hospital deliveries. During the last five years Lowenstein *et al.* (1955), Scott (1957), Cowan (1957), Forshaw *et al.* (1957), and Forshaw (1958) have reported a much higher incidence of this condition. Giles and Shuttleworth (1958) found one case in 39.5 hospital deliveries, and consider this to be an underestimate of the real incidence.

This increase in the described frequency of megaloblastic anaemia of pregnancy is probably due to increased haematological supervision of expectant mothers at antenatal clinics. Formerly a clinical state of severe illness in pregnancy was described, whereas more recent studies are based on haemoglobin levels, irrespective of symptoms and clinical condition of the patients.

Chanarin *et al.* (1959) produce convincing evidence that megaloblastic anaemia of pregnancy is due to a deficiency brought about by poor absorption of folic acid by the mother or by insufficient dietary supply to meet the needs of mother and foetus. In any deficiency disease, for every case of severe deficiency there must be many cases in which the lack is moderate or even very slight. Goodall (1957) describes cases of moderate anaemia of pregnancy without megaloblastic erythropoiesis but which respond only to folic acid. On the other hand, we have found cases with megaloblastic marrows without anaemia, and because of this we have attempted to assess the frequency of this condition by regular haematological studies on all patients attending antenatal clinics at Sunderland Maternity Hospital over the period of 12 months from September, 1958, to September, 1959.

Method

To reduce the incidence of iron deficiency all patients were given routine oral iron (usually "fergon" tablets, one thrice daily) at first attendance at the antenatal clinic when a haemoglobin estimation was performed. At about the 30th week of pregnancy a further haemoglobin estimation was done, and patients with a level of 70% (10 g./100 ml.) or less had P.C.V. and M.C.H.C. estimations and a stained blood film was examined. Patients showing iron deficiency were given 1 g. intramuscular iron ("imferon") in four divided doses and were re-examined in four weeks (haemoglobin, P.C.V., M.C.H.C., and blood film). On admission to hospital at term or for other obstetrical reasons a haemoglobin and blood film from all mothers was examined.

At any stage particular attention was paid to the following features in the blood films.

1. A normochromic normocytic film with haemoglobin below 70% even after intramuscular iron therapy.
2. Hypersegmented neutrophils.
3. Howell-Jolly bodies.
4. Large erythrocytes (macrocytes), even though they be few.
5. Numerous very large fully haemoglobinized erythrocytes, usually about 12 μ in diameter, were sometimes found after intramuscular iron therapy. This "exaggerated response" to iron is strikingly different from the normal response to iron. It is almost certainly the same feature described by Scott (1954) after intravenous iron therapy in some cases of antenatal anaemia.

If one or more of these features were seen in any blood film a marrow biopsy was carried out.

At least four marrow smears were stained by the May–Grünwald–Giemsa method or by Leishman's stain. Marrow fragments aspirated were sectioned, using the method of Cappell *et al.* (1947), and stained with haemalum and eosin and for iron (Hutchison, 1953).

Results

Marrow Findings.—During the 12 months there were 1,996 hospital deliveries, and 95 marrow biopsies were performed for one or more of the reasons mentioned. 73 cases showing megaloblastic erythropoiesis (40 frankly so, and 33 showing transitional or intermediate change). Two further cases without marrow biopsies are included in the series; both had severe anaemia with megaloblasts in the peripheral blood. The incidence of megaloblastic erythropoiesis is therefore 1 case in 26.6 deliveries. Of the 73 megaloblastic marrows, 56 were associated with a marked cellular hyperplasia and virtually complete absence of fat spaces; the remaining 17 showed a normal histological picture. Iron could be demonstrated in 16 cases only (10 frankly megaloblastic and 6 transitional); the amount was always very small.

Degree of Anaemia.—73% of cases with megaloblastic erythropoiesis had a haemoglobin level in the 50–70% range at the time the marrow biopsy was made (Fig. 1).

Age Incidence.—It is considered that the higher age groups tend to develop megaloblastic anaemia more readily than younger subjects. This series tends to confirm this point of view (Fig. 2): 43 cases (57%) were between 18 and 28 years of age, and 32 cases (43%) were 29 years or more. In common with many maternity departments, most admissions are primiparae, and hence tend to be younger: only 30% of admissions to Sunderland Maternity Hospital are 29 years or more.

Parity and Twin Pregnancies.—The parity of 71 mothers was known: 17 were primiparae, 12 were in the second pregnancy, and 16 in the third pregnancy, while the remaining 26 were pregnant for the fourth time or more. 12 cases of megaloblastic erythropoiesis occurred in mothers who had twin pregnancies: during the period of review there were 50 twin births, an incidence of 24% showing megaloblastic erythropoiesis.

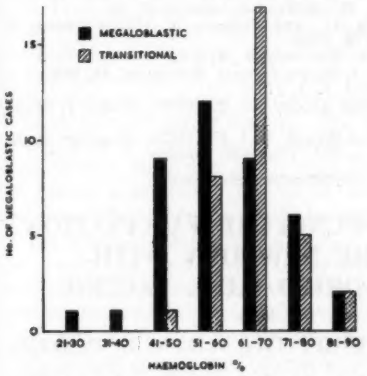

FIG. 1.—Degree of anaemia at time of diagnosis.

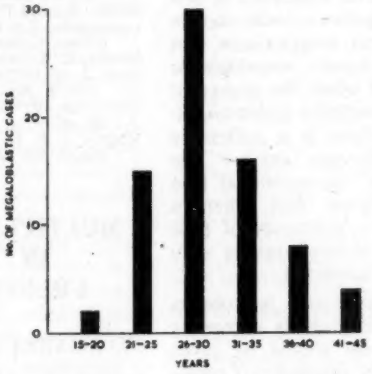

FIG. 2.—Age of incidence.

Time of Diagnosis.—60% of all cases were diagnosed within the period of 10 days before to 10 days after delivery (Fig. 3).

Blood Groups.—The ABO blood group of 67 cases was known (Table I). From this series there does not appear to be any significant association between the liability to develop megaloblastic erythropoiesis and the ABO blood group system. In Addisonian pernicious anaemia there is a significant increase in the incidence of blood group A.

TABLE I.—*ABO Blood Group Distribution of 67 Cases with Megaloblastic Erythropoiesis*

Group A	25 (37·3%)	Group O	30 (44·8%)
„ B	7 (10·4%)	„ AB	5 (7·5%)

TABLE II.—*Number of Cases with Megaloblastic Erythropoiesis During Each Month of Investigation. Total Deliveries are Given in Parentheses*

September	5 (187)	March	8 (168)
October	5 (184)	April	5 (158)
November	4 (136)	May	7 (160)
December	4 (161)	June	9 (168)
January	10 (171)	July	7 (170)
February	4 (151)	August	7 (182)

Seasonal Incidence.—The month in which diagnosis was made did not seem to be significant (Table II).

Complications.—In 68 cases where details were known, 4 (6%) had antepartum haemorrhage, while 29 (42.5%) showed some degree of pre-eclamptic toxaemia. The overall incidence in the unit for antepartum haemorrhage is 2.7% and for pre-eclamptic toxaemia 12.7%. The average haemoglobin level of the 29 cases showing toxaemia was 60%, while the average of 35 cases not showing toxaemia was 61%.

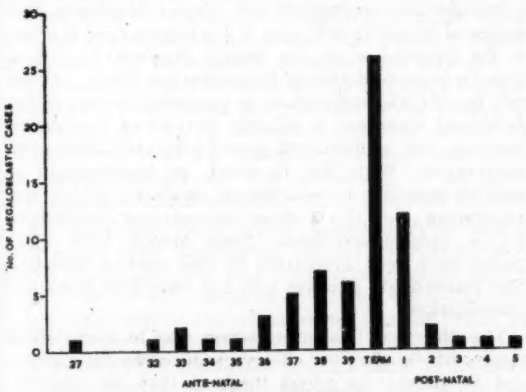

FIG. 3.—Time of diagnosis.

Discussion

This investigation is concerned with the incidence of megaloblastic erythropoiesis in a maternity unit and not with megaloblastic anaemia *per se*. Marrow biopsies were performed on many patients who would not normally be regarded as anaemic; in four cases the haemoglobin was between 80% and 90%. The decision on whether a biopsy was desirable was largely dependent on the appearances of the peripheral blood, and our experience has been that macrocytes in the peripheral blood indicate the possibility of megaloblastic erythropoiesis whatever the haemoglobin level. Megaloblastic anaemia can occur without obvious macrocytosis in the peripheral blood, and because of this our estimate of the incidence of megaloblastic erythropoiesis may be too low; but if patients with a haemoglobin of 65% or less had been selected, as in the series of Giles and Shuttleworth (1958), the incidence would have been 1 case in 38.5 deliveries, a close approximation to the 1 case in 39.6 deliveries which they reported.

In general, interpretation of marrow smears presents little difficulty, but in a few cases prolonged study is necessary. While the differentiation between megaloblastic and transitional erythropoiesis may be convenient for classification, it is nevertheless artificial and seems to be largely a question of degree. Similarly, macronormoblastic erythropoiesis shades into transitional type, and the actual classification eventually depends on individual opinion. In the difficult case the quality of the staining is of the utmost importance, and three or four different smears should be studied. Giant metamyelocytes or giant stab cells and nucleated erythrocytes containing Howell–Jolly bodies (Hutchison

and Ferguson-Smith, 1959) are easily recognized, and are usually indications that megaloblastic changes are present.

The significance of the transitional (intermediate) megaloblast has been the subject of controversy: Dacie and White (1949) and Mollin (1959) believe that transitional megaloblasts are the characteristic marrow reaction where minor deficiencies of vitamin B_{12} or folic acid are present. Fudenberg and Estren (1958) argue that these cells occur because of a superadded deficiency of iron where a deficiency of folic acid or vitamin B_{12} already exists. With both these points of view Kondi and Foy (1959) disagree, as they describe cases of severe anaemia in which only transitional cells can be found, and state that transitional changes are no more frequent in India, where iron deficiency is very common, than in Africa, where iron deficiency is less common. In our experience patients with severe anaemia usually show unequivocal megaloblasts, but this is not always so; conversely, frankly megaloblastic erythropoiesis is sometimes found when the degree of anaemia is slight. Furthermore, we have found transitional-type erythropoiesis where there is a sufficiency of iron and also where a deficiency exists. The "exaggerated macrocytic response" to parenteral iron described by Scott (1954) suggests that when a deficiency of iron in addition to a deficiency of folic acid exists, a macrocytic blood picture appears only when the iron deficiency is being corrected.

Megaloblastic erythropoiesis in pregnancy is probably due to deficiency of folic acid, and there is a growing volume of opinion that folic acid should be given routinely to all cases of anaemia of pregnancy (Lowenstein *et al.*, 1955; Francis and Scott, 1959; Baines, 1959), though opinions vary regarding what haemoglobin level constitutes anaemia. As many of the cases in this series showed only slight anaemia and were detected only just before or just after delivery, the anaemia might have undergone spontaneous remission. This is not always so, as cases of severe megaloblastic anaemia are sometimes not detected until the puerperium.

In this series there have been many cases which showed obstetrical complications other than anaemia; it may be that these complications are aggravated by folic-acid deficiency.

Badenoch *et al.* (1955) suggest that toxaemia may cause anaemia by reducing the ability of the mother's intestine to absorb haemopoietic factors. Another view is that anaemia may be a factor in the development of toxaemia. It might therefore be expected that mothers who develop pre-eclamptic toxaemia would be more anaemic than those who do not. In this series there has been no difference in the average haemoglobin level of the two groups, yet the association between megaloblastic erythropoiesis and toxaemia is high and seems to merit further study.

Summary

In an attempt to find the incidence of megaloblastic erythropoiesis in a maternity unit routine study of blood smears was carried out on antenatal patients showing anaemia and on all patients admitted to the maternity hospital. Marrow biopsies were carried out on all patients showing abnormality of the blood films other than cases of hypochromic anaemia. The incidence of megaloblastic erythropoiesis was found to be 1 case in 26.6 deliveries and 1 case in 4.2 twin deliveries. The condition exists frequently without significant anaemia.

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MULTIPLE-PUNCTURE VACCINATION IN THE NEWBORN WITH FREEZE-DRIED B.C.G. VACCINE

BY

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B.C.G. vaccination has been available in Great Britain for 10 years, and its use in certain groups in the community is now generally accepted. During this period 17,500 newborn infants have been vaccinated with B.C.G. in the University Department of Child Health at St. Mary's Hospital, Manchester. At the outset fresh Danish vaccine was used almost entirely, except for a small amount of freeze-dried vaccine prepared at the Pasteur Institute in Paris, which was kept in readiness as a standby in case the fresh supply should at any time fail. In 1955 a British freeze-dried vaccine was introduced into our immunization scheme, and has now replaced liquid vaccines. In doses of 100.000 to 400,000 viable organisms, given intradermally, it has been found to be effective and free from complications.

Intradermal vaccination will always require a high degree of technical skill, and, if too large a dose is given, or the injection made too deeply, glandular complications or local cold-abscess formation are likely. As the call for B.C.G. vaccination is increased in the underdeveloped countries, a reliable method of inoculation requiring less medical skill would obviously offer great advantages. With this in mind, an investigation of multiple-puncture vaccination of newborn infants was undertaken; for this a more concentrated freeze-dried B.C.G. vaccine was used. Since March, 1958, 2,221 babies have been inoculated by this method, which is now increasingly effective and has been free from any complications.

The object of this investigation was to assess those factors which affect the allergy produced by the vaccine, and to attempt to adjust them so that the multiple-puncture technique could be as effective as the intradermal.

Method

Each ampoule of the special freeze-dried vaccine contained 25 mg. moist weight of B.C.G., which was resuspended in 0.2, 0.3, or 0.5 ml. of sterile water, giving a resultant concentration of 125, 83, and 50 mg./ml., respectively. The most-concentrated suspension was applied to the skin by means of a stainless-steel spatula, and the weaker suspensions were ejected on to the skin from a tuberculin syringe with a fine needle.

Initially, an ordinary Heaf multiple-puncture apparatus, designed for tuberculin-testing (Heaf, 1951) and firing six needles to a depth of 1 mm. or 2 mm., was used. By rotating the base-plate through 30 degrees and firing again, 12 punctures could be administered.

For 20 punctures, Type A guns at variable pressure, and Type B standard-pressure guns, were used. The Type A Mark II gun was designed with 20 individually replaceable needles and a fixed firing penetration of 2 mm.; the Mark III gun also had replaceable needles, but could be adjusted to fire at 1, 2, or 3 mm., and had a much stronger spring loading. The Type B standard-pressure guns fired a fixed number of needles, either 6 or 20, to a depth of 2 mm.; these guns were designed to fire at a constant pressure to eliminate variation between different operators (Carpenter, 1955).

The guns were sterilized before each session by boiling or autoclaving, and during the session were sterilized between each inoculation by immersing the base-plate and needle tips in a mixture of ether 25%, ethyl alcohol 50%, and water 25%, for not less than 30 seconds and then shaking off the surplus moisture. At the end of a session, in which 20 to 30 individuals were vaccinated, the base-plate and needle tips were wiped on blood-agar plates, which were then cultured. All the resulting cultures were found to be free from contaminants. The spirit–ether mixture had no adverse effect on the B.C.G. vaccine.

All injections were made into the right upper arm in the deltoid region in order to leave the left arm free for other immunization procedures.

The skin was cleaned with ether and a drop of vaccine placed on the skin. The base-plate of the gun was then used to spread the vaccine evenly over the skin and ensure that all the holes in the base-plate were covered with vaccine. With the arm held by the left hand, the gun was fired firmly and evenly with the right. The excess of vaccine was then wiped off with a sterile swab.

Initially, comparisons were made in a small series of cases to assess the importance of the size of the drop of vaccine and the effect of wiping off the surplus and sterilizing the base-plate of the gun in spirit–ether–water mixture. It was found that the size of the drop was immaterial so long as there was sufficient vaccine to spread evenly over the base-plate, and that wiping off the surplus vaccine and the sterilization of the base-plate and needles did not impair the effect of the vaccine.

All the infants were given appointments to return four weeks after vaccination. About one-half to two-thirds of the mothers kept these appointments, and a further 30 to 40% returned at a later date. At this visit the inoculation site was inspected and the Mantoux 100 T.U. test was performed, being read in 48 hours. The lesion at the vaccination site consisted of macules or papules which occasionally scaled and sometimes became confluent. In the small number of cases in which lesions were pustular, ulceration never occurred. The resultant scars were almost invisible, and no case of axillary abscess or adenitis has been recorded. A further appointment was made for all the children one year after vaccination; at this visit a Mantoux test 10 T.U. was performed, and, if negative, was followed by 100 T.U.

Results

Number of Punctures and Depth of Penetration.—At the outset the ordinary Heaf multiple-puncture apparatus with six needles, adjustable to fire at a depth of 1 or 2 mm., as devised for tuberculin-testing, was used. The first vaccinations were performed at a depth of 1 mm., the gun being fired once, and in some cases rotated and fired again to produce 12 punctures. For the 20 punctures special models of the guns were made. The results of these investigations are shown in Table I.

TABLE I.—*Effect of Number of Punctures and Depth of Penetration*

Depth	No. of Pricks	100 T.U. at 4 Weeks			10 T.U. at 1 Year		
		No. of Cases	Mean Diameter (mm.)	% Pos.	No. of Cases	Mean Diameter (mm.)	% Pos.
1 mm.	6	23	9·7	91	22	14·1	86
	12	100	10·5	90	99	14·2	88
	20	9			12		
2 „	6	36	11·7	94	31	14·2	97
	12	112	12·4	96	149	15·5	97
	20	105	13·4	98	129	16·7	97

Guns, Type A Mk I (1 mm.) and Type A Mk II (2 mm.). Vaccine Batch P.2

It can be seen that allergy produced at four weeks and persisting to one year gradually improves as the number of punctures is increased, and that the depth of penetration has a more significant effect than the number of punctures. With newer guns and modified needles the results at four weeks have been improved still further (see Table III), and it is considered that 20 punctures at 2 mm. with a suitable gun will produce adequate tuberculin sensitivity in newborn infants.

Concentration of Vaccine.—The results of varying the concentrations are shown in Table II. It would appear that increasing the concentration of vaccine above

TABLE II.—*Concentration of Vaccine*

Batch	Concentration mg./ml.	20 Pricks		6 Pricks	
		No. of Cases	100 T.U. at 4 Weeks (Mean Diameter, mm.)	No. of Cases	100 T.U. at 4 Weeks (Mean) Diameter, mm.
P6	50	54	12·5	—	—
	83	28	12·9	43	12·6
P7	83	68	11·9	23	12·8
	125	96	12·4	53	12·6

Gun used, Type A Mk II. Depth of penetration, 2 mm.

50 mg./ml. does not increase the tuberculin sensitivity produced at four weeks after vaccination. For practical purposes a dilution of 83 mg./ml. is the easiest to use, as it is sufficiently fluid to be delivered from a tuberculin syringe through a fine needle, thus eliminating the need for a spatula or platinum loop, and it is viscous enough not to run off the arm, as the thinner 50 mg./ml. suspension tends to do.

Modification of Guns and Needles.—When it was clear that vaccination was effective at a depth of 2 mm. with 20 punctures, and that the effect was not increased by increasing the strength of the vaccine, other methods of improving the technique were considered. The Type A Mark III guns were made with stronger springs, and the needles were roughened first by grooves and

later by providing tungsten tips. The standard-pressure Type B guns with a needle of larger diameter and shorter bevel were used. The results in Table III show

TABLE III.—*Type of Gun and Needles Used*

Gun	Needles	6 Punctures at 2 mm. — 100 T.U. at 4 Weeks			20 Punctures at 2 mm. — 100 T.U. at 4 Weeks		
		No. of Cases	Mean Induration (mm.)	% Pos.	No. of Cases	Mean Induration (mm.)	% Pos.
Type A Mk II	Smooth	36	11·7	94	105	13·4	98
,, ,, ,, III	,,	60	13·5	95	14	12·8	100
,, ,, ,, III	Rough	111	15·3	100	50	14·8	100
,, ,, ,, III	,, (B type)				34	14·6	100
,, B	Smooth	61	14·8	100	42	14·8	100

Concentration of vaccine, 83 mg./ml. throughout.

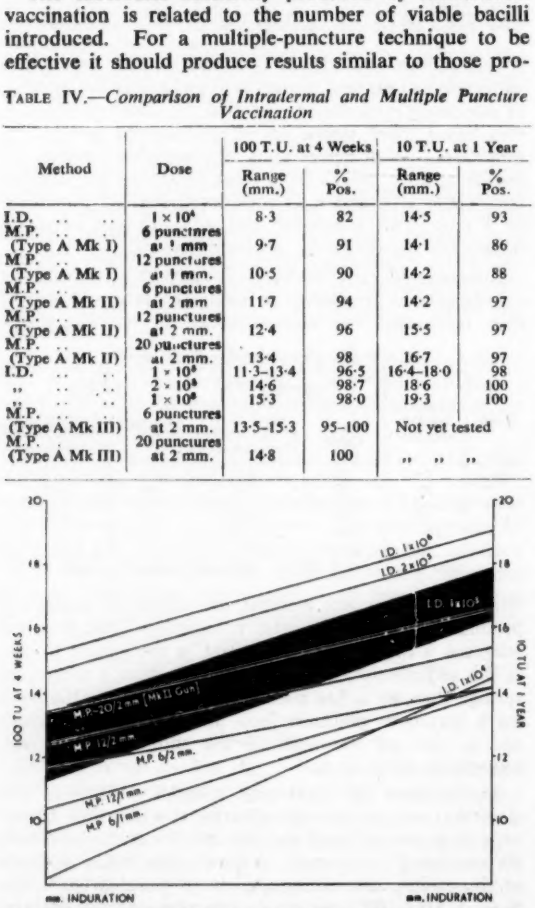
that these modifications have been to some extent effective, and that with either 6 or 20 punctures at 2 mm. the later type gun produces a stronger tuberculin sensitivity at four weeks. It is not yet known whether this improvement will be associated with a longer duration of allergy.

Comparison with Results of Intradermal Vaccination

The tuberculin sensitivity produced by intradermal vaccination is related to the number of viable bacilli introduced. For a multiple-puncture technique to be effective it should produce results similar to those pro-

TABLE IV.—*Comparison of Intradermal and Multiple Puncture Vaccination*

Method	Dose	100 T.U. at 4 Weeks — Range (mm.)	100 T.U. at 4 Weeks — % Pos.	10 T.U. at 1 Year — Range (mm.)	10 T.U. at 1 Year — % Pos.
I.D.	1×10^6	8·3	82	14·5	93
M.P. .. .. (Type A Mk I)	6 punctures at 1 mm	9·7	91	14·1	86
M.P. .. .. (Type A Mk I)	12 punctures at 1 mm.	10·5	90	14·2	88
M.P. .. .. (Type A Mk II)	6 punctures at 2 mm	11·7	94	14·2	97
M.P. .. .. (Type A Mk II)	12 punctures at 2 mm.	12·4	96	15·5	97
M.P. .. .. (Type A Mk II)	20 punctures at 2 mm.	13·4	98	16·7	97
I.D.	1×10^5	11·3–13·4	96·5	16·4–18·0	98
,, ...	2×10^5	14·6	98·7	18·6	100
,, ...	1×10^6	15·3	98·0	19·3	100
M.P. .. .. (Type A Mk III)	6 punctures at 2 mm.	13·5–15·3	95–100	Not yet tested	
M.P. .. .. (Type A Mk III)	20 punctures at 2 mm.	14·8	100	,, ,, ,,	



Comparison of results from intradermal (I.D.) and multiple-puncture (M.P.) vaccination.

duced by the optimal dose injected intradermally (in newborn infants, using British freeze-dried vaccine, this is probably of the order 200,000 to 400,000 viable bacilli per dose). Table IV and the accompanying Graph illustrate the results so far achieved. With the Type A Mark II gun the results of vaccination with 6 punctures at 1 mm., and 6 punctures at 2 mm., are probably inadequate; 12 punctures at 2 mm. show a fall after one year; and 20 punctures at 2 mm. bring results within the range produced by 100.000 bacilli given intradermally. With newer guns (Type A Mark III and Type B standard-pressure type) firing 20 needles, the tuberculin sensitivity produced at four weeks is within the range produced by the intradermal injection of 200.000 to 400,000 bacilli. It remains to be seen whether the tuberculin sensitivity at one year continues to be adequate.

Discussion

Conflicting results with regard both to intradermal and to multiple-puncture vaccination may be attributed to variations in antigenicity and potency of the vaccine and in the technique of application.

Although any B.C.G. vaccine applied by any method may produce tuberculin sensitivity and a degree of protection against tuberculosis in some of the subjects vaccinated, it is desirable that these results should be as effective and long-lasting as possible. Using the British freeze-dried vaccine intradermally, it has been possible to correlate to some degree the clinical effects of vaccination with the dose of viable bacilli administered (Griffiths, and Gaisford 1956; Ungar, 1958; Griffiths, 1960), and similar results have been reported with the Japanese vaccine (Obayashi *et al.*, 1959). With multiple puncture vaccination, on the other hand, it is impossible to make any assessment of the number of viable organisms entering the skin, and it is only possible to assess their practical importance by varying some of the factors involved.

Number of Punctures.—Rosenthal (1957) thought that 18 to 36 punctures were essential and found a correlation between clinical effectiveness and number of punctures. Lorber (1959) also noted the importance of this factor. In the present series the increase in tuberculin sensitivity, particularly immediately after vaccination, produced by increasing the number of punctures from 6 to 20 was much less than one would have expected. However, since duration of allergy seemed to be related rather to the number of punctures, it has been decided that 20 punctures should be the routine procedure for vaccination in the newborn at the present time.

Depth of Penetration.—Lorber (1959) suggests that a depth of 1 mm. is sufficient for vaccination in infancy. From the experience in this series there appears to be no doubt that a penetration of 2 mm. gives better results than 1 mm., particularly in the results of tuberculin testing at a later date. This would seem reasonable in that the thickness of the epidermis in newborn infants is such that one would expect penetration of 2 mm. to be the optimum to reach those layers of the corium with adequate lymphatic communications.

Concentration of Vaccine.—Ejlersen (1953) and Rosenthal (1957) have shown that improved clinical effects can be expected by increasing the concentration of vaccine. In both these reports the range of concentration was from 5 mg./ml. to 50 mg./ml., well below the concentration studied in this present series. It therefore seems likely that a concentration over 50 mg./ml. is

adequate and that it is almost impossible to get a concentration that will produce glandular complications so common with higher doses of intradermal vaccine. Practical reasons for preferring a dosage of 83 mg./ml. have already been mentioned.

Modification of Guns and Needles.—This is a factor which has received very little attention in previous reports. First attempts at multiple-puncture vaccination (Rosenthal, 1939; Rosenthal and Neiman, 1941) by means of 20 to 30 tangential pricks from a single needle were followed by use of Birkhaug's instrument (Birkhaug, 1947), of which the Heaf (1951) multiple-puncture apparatus would seem to be a simple modification. The present Rosenthal technique (Rosenthal, 1957) utilizes a disk with 36 points and does not depend on any spring pressure. At the moment we are interested in the question of the physical factors involved in firing the gun, and this will be discussed in a later paper; it is quite evident, however, that the technique of multiple-puncture vaccination must be as meticulous as that for the intradermal method even though it calls for less basic skill.

Comparison with Results of Intradermal Inoculation.—Previous reports on the relative efficiency of intradermal and multiple-puncture vaccination have been conflicting. Rosenthal (1939) and Rosenthal and Neiman (1941) consider that multiple puncture vaccination is as effective as intradermal and indeed offers more complete protection against tuberculosis. Ejlersen (1953) takes the opposite view. In the present series the aim has been to improve the technique of multiple-puncture vaccination so that it is, as nearly as possible, as effective as the intradermal vaccination with freeze-dried vaccine.

Summary

A total of 2,221 newborn infants have been inoculated with British freeze-dried B.C.G. vaccine by multiple-puncture vaccination between March, 1959, and April, 1960.

Details of technique are described and significant factors discussed.

The results of multiple-puncture vaccination are compared with those of intradermal vaccination.

It is suggested that, using the British freeze-dried vaccine, optimal results are obtained by firing 20 needles to a depth of 2 mm. through a vaccine concentration of 83 mg./ml. It is hoped that by further improvement in technique the efficiency of multiple-puncture vaccination may be raised to the standard produced by intradermal vaccination.

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OBSERVATIONS ON VACCINATING SCHOOLCHILDREN WITH DANISH FRESH B.C.G.

BY

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In 1954 eight medical officers of health in the Oxford Region adopted a uniform procedure for the testing and B.C.G. vaccination of their schoolchildren. The scheme was in full operation by 1955. In that year, however, the P.P.D. issued for routine Mantoux testing was sub-standard. The findings have therefore been analysed from 1956 onward. The overall conversion rates for that year have already been published (Irvine, 1958). In this report the conversion rates and the local reactions to vaccination are studied in greater detail.

Material and Method

The analysis is based on 8,990 routine B.C.G. vaccinations of 13-year-old schoolchildren in the Oxford Region during the school year 1956-57. Mantoux 10 T.U. tests were given for the pre- and post- vaccination tests in 5,390 children and Heaf multiple-puncture tests in 3,600. The standard preparations of P.P.D. issued by the Ministry of Health were used for each test. Both Mantoux and Heaf tests were read at 2 to 4 days; the criterion of a minimum positive reaction for the Mantoux was an area of induration whose diameter was 6 mm., and for the Heaf test induration at four punctures. Non-reactors were vaccinated intracutaneously by some 50 school medical officers with 0.1 ml. of Danish fresh vaccine (0.75 mg./ml.), using about 40 different batches. The post-vaccination test was carried out between 6 and 19 weeks after vaccination. The local reaction to vaccination was inspected at the time of the post-vaccination test, and the diameter in millimetres of the indurated papule was measured with callipers; all Mantoux reactions were also measured with callipers. Where a vaccination or Mantoux reaction was not circular, the measurement recorded was the mean of the largest and the smallest diameter. None of the children was in contact with known open tuberculosis at the time of vaccination.

Results

Hertzberg (1948) found that sex had no influence on the size of the vaccination reaction or the conversion rate. An initial analysis of the present data provided similar results, and this factor has accordingly been ignored in the study.

Conversion Rate.—This has been analysed according to the number of weeks elapsing since vaccination. The

TABLE I.—*Analysis of Local Reactions to B.C.G. Vaccination*

Series	Weeks after Vaccination:	6		7		8		9		10		11		12		13		14		15		16		17		18		19		All		Total Vaccinations	Conversion Rate (%)
	Converters (+); Non-converters (−):	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−		
Mantoux 10 T.U.	Local reaction to vaccination (mean diameter of papule in mm.) 0	—	—	1	—	—	3	2	5	—	2	8	1	4	6	1	—	—	—	—	—	—	1	1	2	10	—	—	—	27	17	44	61·4
	1–	—	—	29	—	53	1	24	6	45	5	48	23	151	6	61	3	20	—	20	2	6	1	33	2	1	—	—	—	491	52	543	90·4
	6–	—	—	237	6	729	12	420	15	285	6	356	6	768	18	429	10	234	—	198	4	25	—	313	16	71	1	—	—	4,065	93	4,158	97·8
	11–	—	—	68	—	148	—	81	2	47	1	33	—	70	3	15	1	20	—	23	—	2	—	39	—	27	1	—	—	573	8	581	98·6
	16+	—	—	5	—	21	—	13	—	10	—	3	—	9	—	1	—	1	—	1	—	—	—	—	—	—	—	—	—	64	—	64	100·0
	All	—	—	340	18	951	9	540	28	387	9	448	30	1,002	33	507	15	275	—	242	6	33	2	386	18	109	2	—	—	5,220	170	5,390	96·8
	*Mean diameter (mm.)	—		9·15		9·20		9·21		8·91		7·85		8·07		7·85		8·32		8·50		7·61		8·13		9·02		6·79		8·54			
	Standard error of mean (mm.)	—		0·14		0·09		0·12		0·17		0·14		0·08		0·08		0·12		0·13		0·40		0·11		0·35		—		0·04			
	Standard deviation (mm.)	—		2·63		2·66		2·90		3·35		2·57		2·62		1·85		2·01		2·12		2·35		2·15		3·69		—		2·66			
	Conversion rate (%)	—		95·0		99·1		95·1		97·7		93·7		96·8		97·1		100·0		97·6		94·3		95·5		98·2				96·8			
	Conversion rate (%) omitting "0" vaccination reaction	—		95·0		99·4		95·7		97·7		93·4		97·3		97·2		100·0		97·6		97·0		95·5		98·0		—		97·1			
Heaf	Local reaction to vaccination (mean diameter of papule in mm.) 0	1	21	4	13	16	12	8	18	1	2	—	—	2	—	1	—	—	—	2	1	—	—	1	—	—	—	—	—	36	67	103	35·0
	1–	164	1	224	4	152	—	136	—	52	—	21	—	4	—	9	—	23	—	32	1	35	1	21	—	43	2	1	—	971	6	977	99·4
	6–	154	1	163	—	88	—	99	—	31	—	23	—	25	—	112	—	240	—	380	1	325	—	152	—	295	2	55	—	2,198	5	2,203	99·8
	11–	43	—	12	—	10	—	38	1	5	—	—	—	2	—	6	—	25	—	43	—	38	—	9	—	37	2	111	3	271	3	274	98·9
	16+	2	—	2	—	7	—	14	1	2	—	—	—	—	—	1	—	2	—	4	—	3	—	—	—	4	—	1	—	42	1	43	97·7
	All	364	23	405	17	273	12	295	20	91	2	44	—	83	—	129	—	290	—	461	2	401	2	183	—	379	4	170	—	3,518	82	3,600	97·7
	*Mean diameter (mm.)	6·93		5·70		5·68		6·98		6·27		6·20		7·80		8·00		8·60		8·63		8·69		8·02		8·46		6·79		7·47			
	Standard error of mean (mm.)	0·18		0·13		0·23		0·28		0·34		0·27		0·49		0·18		0·13		0·10		0·11		0·18		0·12		0·14		0·05			
	Standard deviation (mm.)	3·48		2·65		3·94		4·89		3·23		1·79		2·79		2·03		2·17		2·24		2·25		2·40		2·29		1·79		3·15			
	Conversion rate (%)	94·1		96·0		95·8		93·7		97·8		100·0		100·0		100·0		100·0		99·6		99·5		100·0		99·0		100·0		97·7			
	Conversion rate (%) omitting "0" vaccination reaction	99·5		99·0		100·0		99·3		100·0		100·0		100·0		100·0		100·0		99·8		99·5		100·0		99·0		100·0		99·6			

* Means, standard errors, and standard deviations were calculated on the actual diameter of the vaccination reaction.

results are summarized in Table I. The post-vaccination tests for the Mantoux series fall by chance between 7 and 18 weeks after vaccination and for the Heaf series between 6 and 19 weeks. The overall conversion rate for the Mantoux series was 96.8%, the weekly conversion rate ranging between 93.7 and 100%. Within this period there was no indication that the conversion rate was affected by the length of time between vaccination and post-vaccination testing. The overall conversion rate for the Heaf series was 97.7%. There was little difference, therefore, between the Heaf and Mantoux tests in this respect. The weekly conversion rate ranged between 93.7 and 100%; from 6 to 11 weeks the rate increased slightly, thereafter the range being between 99 and 100%.

Local Reaction to Vaccination.—An analysis has been made at weekly intervals to determine whether there was any alteration in the diameter of the vaccination papule during the period under observation (Table I). In the Mantoux series the vaccination papule had an overall mean diameter of 8.5 mm. The weekly mean diameter from 7 to 18 weeks ranged between 7.6 and 9.2 mm., which indicated that there was little change in the diameter of the vaccination reaction during the period of observation. In the Heaf series the findings were similar. The overall mean diameter was 7.5 and the weekly mean diameter from 6 to 19 weeks ranged between 5.7 and 8.7 mm.—a range of 3 mm. There was a slight tendency for the range to be larger from 6 to 14 weeks, but from 12 to 19 weeks it was less than 2 mm.

Relationship between Local Reaction to Vaccination and Conversion Rate.—Inspection of the local reaction to vaccination is a simpler procedure than giving and reading a post-vaccination tuberculin test. An analysis has therefore been made to determine whether there was any relationship between the vaccination reaction and the conversion rate. In the Mantoux series, 5,346 children had vaccination reactions ranging from 1 to 40 mm. in diameter; of these, 153 (2.9%) failed to convert, giving a conversion rate of 97.1%. In addition, there were 44 children who had no vaccination reaction; of these, 17 (38.6%) failed to convert, giving a conversion rate of 61.4%. In the Heaf series, 3,497 children had vaccination reactions ranging from 1 to 32 mm. in diameter; of these, only 15 (0.4%) failed to convert, giving a conversion rate of 99.6%. In addition, there were 103 children who had no vaccination reaction; of these, 67 (65%) failed to convert, giving a conversion rate of only 35%. In both the Mantoux and the Heaf series failure to convert was uncommon among children with a recognizable local reaction to vaccination. In

children with no local vaccination reaction, failure to react is comparatively frequent. This association is more evident with the Heaf test. The Mantoux series was further analysed to determine whether the diameter of the vaccination reaction bore any relationship to the diameter of the Mantoux reaction. Table II shows that the vaccination and Mantoux reactions increased uniformly. This is in accordance with the findings of Hertzberg (1948).

TABLE II.—*Mean Diameter of Post-vaccination Mantoux Reaction for Different Diameters of Vaccination Reaction*

Local Reaction to Vaccination (Mean Diameter of Papule in mm.)	Mantoux 10 T.U. P.P.D. Reaction			No. of Children*
	Mean Diameter (mm.)	Standard Error of Mean	Standard Deviation	
1–} 2–}	8·2	0·66	1·64	6
3–	9·8	0·53	2·55	23
4–	9·7	0·25	2·45	99
5–	10·1	0·16	2·94	354
6–	11·0	0·11	3·26	838
7–	11·2	0·11	3·28	926
8–	11·8	0·10	3·19	1,023
9–	12·6	0·14	3·51	396
10–	12·8	0·14	3·40	618
11–	12·7	0·27	3·48	168
12–	13·1	0·26	3·85	215
13–	13·2	0·49	3·24	43
14–	13·8	0·41	3·69	82
15–	14·5	0·52	4·14	64
16–	13·5	0·29	2·31	63

* Excludes children whose Mantoux reaction was not read or not reported.

Discussion

The findings described above relate to the diameter of the vaccination reaction and the conversion rate at different intervals after vaccination. Approximately 9,000 children were concerned, each of whom was examined once only at intervals after vaccination ranging from 6 to 19 weeks. The vaccination lesions and tuberculin reactions have been analysed according to the period after vaccination at which the examinations were made. The analysis is therefore a number of cross-sections at different time intervals and not a serial investigation of conversion rates.

In the Mantoux series no change was observed in the conversion rate between 7 and 18 weeks after vaccination. In the Heaf series an increase in the conversion rate was noted in children tested after 11 weeks as compared with those tested between 6 and 11 weeks after vaccination. However, 96 of the children tested between 6 and 11 weeks had no vaccination reaction. If all children with no vaccination reaction are excluded from the analysis, the overall conversion rate for the Heaf series becomes 99.6% and shows no upward or downward trend. These findings suggest that the conversion rate to a Mantoux or Heaf test is not greatly affected by the time elapsing since vaccination within a range 6 to 19 weeks.

Similarly, the diameter of the vaccination papule remains constant from 6 to 19 weeks, the mean varying only within the narrow range of 3 mm. Thus valid comparisons may be made between the vaccination reaction and the conversion rate to a Mantoux 10 T.U. carried out between 7 and 18 weeks, or to a Heaf test carried out between 11 and 19 weeks.

The relationship demonstrated between the local reaction to vaccination and the conversion rate in the Heaf series is striking; only 0.4% of children with vaccination reactions failed to convert. Similarly, the association found between the diameter of the vaccination papule and of the Mantoux reaction is marked. It must, however, be borne in mind that this relationship has been shown only for Danish fresh vaccine, a vaccine whose potency and effectivenesss has already been demonstrated (Medical Research Council, 1959). As the proportion of dead organisms is increased in a vaccine, the conversion rate declines more rapidly than the associated decrease in the diameter of the local reaction (Edwards, Palmer, and Magnus, 1953). Thus in vaccines of known potency the vaccination reaction is a useful guide to the likelihood of tuberculin conversion having been achieved. This relationship may not hold good for vaccines of inferior potency. Provided that Danish fresh vaccine maintains its past standards, it seems reasonable to suggest that, where evidence of successful vaccination is required, inspection of the vaccination site at or after 11 weeks could replace conversion testing. A test would then only be required for those vaccinations that have no local reaction.

Summary and Conclusion

In the Oxford Region 8,990 13-year-old schoolchildren were vaccinated with Danish fresh B.C.G. during the school year 1956-7; in 5,390 children the pre- and post-vaccination test was a Mantoux 10 T.U. P.P.D. and in 3,600 the Heaf multiple-puncture test was used. An analysis of the conversion rate and of the size of the local reaction to vaccination was made according to the interval in weeks (6–19) after vaccination.

In the Mantoux series the conversion rate between 7 and 18 weeks after vaccination remained within the range 93.7 to 100% and showed no tendency to decline or increase. In the Heaf series the conversion rate rose from 94.1% at six weeks to between 99 and 100% from 11 to 19 weeks; this increase in the conversion rate with the Heaf test was probably not due to the interval from vaccination.

The average diameter of the local reaction to vaccination did not vary by more than 3 mm. in either series over the period of observation.

In the Heaf series the conversion rate of those who had no local reaction was 35%; in those who had a local reaction, however small, the conversion rate was 99.6%. In the Mantoux series it was found that the diameter of the Mantoux reaction had a direct relationship to the diameter of the vaccination papule.

The presence of any local reaction to intracutaneous vaccination with Danish fresh vaccine may be regarded as an indication of successful vaccination. Only persons with no local reaction to vaccination require a conversion test.

The figures for this paper are taken from the special records kept by the eight local health authorities in the Oxford Region who now form the B.C.G. Control Centre: Berkshire, Gloucestershire, Northamptonshire, Oxfordshire, and Wiltshire County Councils, and Northampton, Oxford, and Reading County Borough Councils; we thank all the medical officers of health and school medical officers concerned. We are particularly grateful to Dr. T. M. Pollock and Dr. I. Sutherland, of the Medical Research Council, who read and criticized the original draft of this paper. We also thank the staff of the records and statistics department of the Oxford Regional Hospital Board for their co-operation. One of us (K.N.I.) is indebted to the Medical Research Council for grants towards this research.

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CLINICAL ASSESSMENT OF MITRAL ORIFICE IN PATIENTS WITH REGURGITATION

BY

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AND

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Mitral regurgitation may take place through orifices which are severely narrowed and through orifices which are so large as to offer negligible obstruction. In disabled patients the size of the mitral lumen chiefly determines whether surgical treatment should relieve stenosis or correct incompetence.

A study of 20 patients suffering from mitral regurgitation has suggested that the size of the mitral orifice may be predicted with reasonable accuracy from the cardiac impulse and heart sounds.

Material and Methods

Twenty patients with signs of mitral incompetence and auricular fibrillation were selected for study on the grounds of their freedom from evidence of hypertensive, ischaemic, or aortic valvular disease. At valvotomy or open-heart operation the presence of regurgitation was confirmed and the long diameter of the mitral orifice measured by palpation (G. H. W.).

Pre-operatively, the patients were examined with special reference to the nature of the cardiac impulse, the mitral diastolic murmur, and the third heart sound of rapid left ventricular early diastolic filling. In every patient a crystal microphone and an oscillographic phonocardiograph were used to record the heart sounds at a paper speed of 80 mm./sec. Simultaneous tracings were taken from the pulmonary area (high frequency) and apex (high or medium frequency: Leatham, 1952). Care was taken to avoid filtering or attenuating out the third heart sound and the onset of the mitral diastolic murmur. From the tracings two varieties of passive mitral diastolic murmur were recognized: those with a loud abrupt onset and short duration, and those which were quiet in onset and long in duration.

A third heart sound was regarded as present when vibrations twice the size of the first variety of passive diastolic murmur occurred shortly after its beginning. The identification severally of aortic and pulmonary-valve closure and mitral opening snap vibrations, and the configuration and time relationships of the third sound, distinguished it from other transients. The third heart sound was not commonly present in every cardiac cycle, and its occurrence was noted as being frequent or infrequent. In several patients the third sound was loudest towards the end of expiration. The apical thrust of a palpable left ventricle was recorded as being present or absent.

In 13 patients left atrial pressure pulses were obtained by the method of Allison and Linden (1955) or Ross (1959) at a time when the heart rate was slow enough for diastasis to be demonstrable. Patients with sinus rhythm were excluded from this study.

Results

The important findings are shown in the accompanying Table.

In five cases with orifices measuring 1.2 cm. or less the mitral diastolic murmur began quietly and there was no third sound. Two patients with orifices of 1.5 cm. showed similar features. The mitral diastolic murmur began loudly and a third sound was present occasionally in the third patient with a 1.5-cm. orifice and in the patient with a 1.8-cm. orifice. With orifices of 2 cm. or more the mitral diastolic murmur began very loudly and a third heart sound occurred in the majority of cardiac cycles. The left ventricle was palpable in half the patients with orifices of 1.5 cm. or less and in all the patients with larger orifices. The absence of a late diastolic rise in left atrial pressure indicated severe mitral obstruction in five patients with orifices of 1.5 cm. or less. The presence of such a rise indicated ease of flow from left atrium to ventricle in eight patients with orifices measuring 1.8 cm. or more.

Case	Left Ventricle Palpable	Mitral Diastolic Murmur		Third Heart Sound		Long Diameter of Mitral Orifice (cm.)	Diastasis
		Quiet Onset	Loud Onset	Infrequent	Frequent		
1	+	+	0	0	0	0·5	0
2	+	+	0	0	0	1·0	
3	0	+	0	0	0	1·0	0
4	0	+	0	0	0	1·0	0
5	0	+	0	0	0	1·2	
6	+	+	0	0	0	1·5	0
7	0	+	0	0	0	1·5	0
8	+	0	+	+	0	1·5	
9	+	0	+	+	0	1·8	+
10	+	0	+	0	+	2·0	+
11	+	0	+	0	+	2·25	+
12	+	0	+	0	+	2·25	+
13	+	0	+	0	+	2·5	+
14	+	0	+	0	+	2·5	+
15	+	0	+	0	+	3·0	
16	+	0	+	0	+	3·0	
17	+	0	+	0	+	3·5	
18	+	0	+	0	+	3·5	
19	+	0	+	0	+	3·5	+
20	+	0	+	0	+	4·0	+

The symbols + and 0 represent the presence or absence of the physical sign.
Diastasis is the phase of diastole immediately preceding systole during which the atrial pressure normally rises. The absence of an entry indicates either that the left atrial pressure pulse was not recorded or that tachycardia prevented the possible appearance of this feature

Discussion

The borderline between predominant obstruction and predominant incompetence seems to lie with orifices measuring 1.5–1.8 cm. in diameter. With this order of lumen the left ventricle may or may not be palpable, a third heart sound may appear occasionally or not, the passive diastolic murmur may have a quiet or a loud beginning, and diastasis may or may not be present. With smaller orifices it appears that the mitral diastolic murmur begins quietly, and the third sound does not occur. The absence of a late diastolic rise in left atrial pressure indicates severe obstruction. With orifices measuring 2 cm. or more the left ventricle is invariably palpable, the diastolic murmur has an explosive onset, a third sound is present in most cardiac cycles, and the rise of left atrial pressure in diastasis is a reliable sign that atrium and ventricle can fill together as a common chamber.

The brevity of the mitral diastolic murmur in incompetence contrasted with its length in stenosis has been described by Wood (1956). McKusick (1958)

observed that the passive murmur of mitral stenosis may not fill diastole if the disease is trivial and if heart rate or cardiac output is low. Brandenburg and Burchell (1958) rarely found the passive murmur confined to early diastole in cases of advanced mitral obstruction. McDonald *et al.* (1957) considered that a long diastolic murmur indicated severe stenosis and that a short diastolic murmur was typical of mitral incompetence. Turner and Fraser (1956) thought that the duration of the diastolic murmur was principally determined by the rigidity of the mitral valve. We believe that while the diastolic murmur is generally long in severe mitral stenosis, it may be short in mild mitral stenosis, in mitral regurgitation, and in moderately severe mitral stenosis when the cardiac output and heart rate are low. Furthermore, it may be difficult to measure the length of the diastolic murmur in a patient with a low cardiac output and a thick chest wall.

Hultgren and Leo (1959) and Nixon *et al.* (1959) observed the explosively loud onset of the short mitral diastolic murmur in patients with severe regurgitation (Fig. 1). The third heart sound occurs early in this murmur. It may be difficult to decide whether large vibrations are part of the murmur or whether they form a third sound. The decision is probably of no importance, since each appears to indicate that the orifice is not severely obstructed. This murmur of dominant regurgitation is distinguished more easily from the quietly beginning long-drawn-out murmur of dominant obstruction (Fig. 2) by its loud onset than by its short duration. There may be advantage in naming the former the *high-flow* mitral diastolic murmur, and the latter the *low-flow* mitral diastolic murmur.

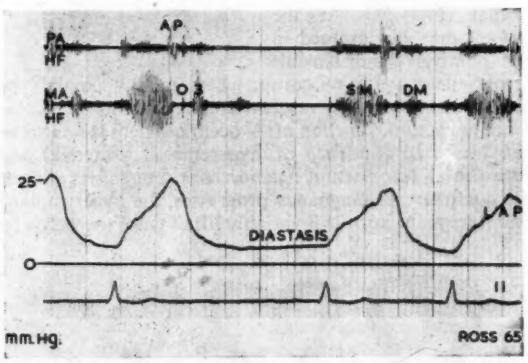

FIG. 1.—Simultaneous high-frequency pulmonary and mitral phonocardiograms, left atrial pressure, and electrocardiogram from a patient with a 2.5 cm. mitral orifice. Diastasis indicates the period in late diastole during which left atrial pressure rises as the left atrium and ventricle fill together as a common chamber.

P.A.=Pulmonary area. M.A.=Mitral area. A.P.=Aortic and pulmonary valve closure. O=Opening snap of mitral valve. 3=Third heart sound of rapid left ventricular filling. S.M.=Pansystolic mitral murmur. D.M.=Mitral diastolic murmur with a loud beginning. H.F.=High frequency.

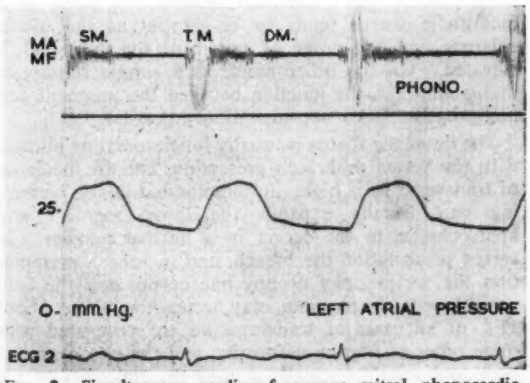

FIG. 2.—Simultaneous medium-frequency mitral phonocardiogram, left atrial pressure, and electrocardiogram from a patient with a mitral orifice measuring 1 cm.

T.M.=Tricuspid followed by mitral valve closure. S.M.=Pansystolic mitral murmur. D.M.=Mitral diastolic murmur with a quiet beginning. M.A.=Mitral area. M.F.=Medium frequency.

Right and left heart pressure pulses and indicator-dilution curves have been obtained in 50 patients disabled from mitral-valve disease, using the method described by Nixon (1960a). This experience has supported the view that the onset of the mitral diastolic murmur is the single feature of greatest value in predicting when regurgitation is too severe for valvotomy to be offered to a patient with atrial fibrillation.

The loudness of the first sound and systolic murmur are not reported in this communication because they appeared to have little value in diagnosing the size of the mitral orifice.

A loud mitral opening snap occurred in 13 of the patients reported here, and in every one the main part of the aortic cusp was supple and capable of ballooning. In one case a faint opening snap was just visible on the phonocardiograph, and the aortic cusp was found to be thickened and moving poorly. There was no opening snap in the remaining six patients in whom the aortic cusp proved to be rigid and immobile. The presence of an opening snap was not related in any way to the size of the mitral lumen. Similar findings have been reported previously (Nixon *et al.*, 1959; Nixon, 1960b).

If future experience supports the observations made in this small group of patients with mitral regurgitation it may become possible to diagnose the size of the mitral orifice and the state of the aortic cusp from the onset of the diastolic murmur and the opening snap.

Summary

A clinical and surgical study of 20 patients with mitral regurgitation and atrial fibrillation suggests that a quietly beginning diastolic murmur identifies a mitral orifice measuring less than 1.5 cm. in diameter. With orifices of 2 cm. or more the diastolic murmur begins loudly and a third heart sound appears frequently.

It is suggested that the former murmur should be named the low-flow mitral diastolic murmur, and the latter the high-flow mitral diastolic murmur.

We are grateful to Mr. R. Addyman and Staff Nurse E. M. Kirkbride for zealous technical assistance.

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PRACTICAL SIGNIFICANCE OF UTERINE DEFORMITIES DURING PREGNANCY AND LABOUR*

BY

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During the past 20 years I have seen 67 cases of major fusion deformity and many cases of minor deformity of the uterus. Of the 67 patients, 32 have each had between one and five viable children. I have therefore had many opportunities for observing the general pattern of pregnancy and labour complicated by different forms of uterine anomaly (Hunter, 1957).

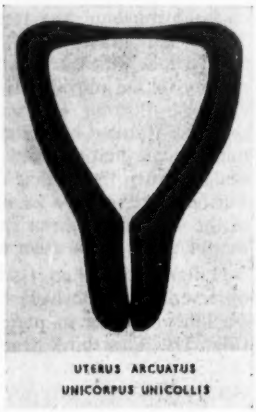
Diagnosis and Terminology

It has become evident that if the precise nature of the deformity is known beforehand it is possible to foretell with some degree of accuracy which complications of pregnancy and labour are apt to occur in any particular case. It is difficult, however, to arrive at a definite anatomical diagnosis in the non-pregnant state and still more difficult during pregnancy. The presence of a uterine deformity may be suggested by the finding of a vaginal septum; and the diagnosis is based upon the findings on vaginal examination with palpation and inspection of the cervix; uterine palpation, exploration of the cervical canal and uterine cavity with a sound; hystero-salpingography; and, when the operation is necessary for some coincident condition, laparotomy. During late pregnancy the presence of a transverse foetal lie or of an oblique lie with the head or breech in one cornu and the feet in the other suggests that there may be a single but deformed uterine cavity; and the presence of a slender extended breech in a somewhat elongated uterus inclined to one side and a high presenting part suggests that there may be two separate, non-communicating uterine cavities. Palpation of the uterine cavity during manual removal of a retained placenta may give useful information about its conformation.

The terminology used in describing cases of fusion deformities of the uterus should be informative and precise. The state of the uterine fundus, of the uterine cavity, and of the cervical canal should always be indicated in the descriptive term used in the records if this term is to be sufficiently comprehensive to be of value in future attempts to foretell the outcome of any particular case (Hunter, 1950).

Single Uterine Cavity

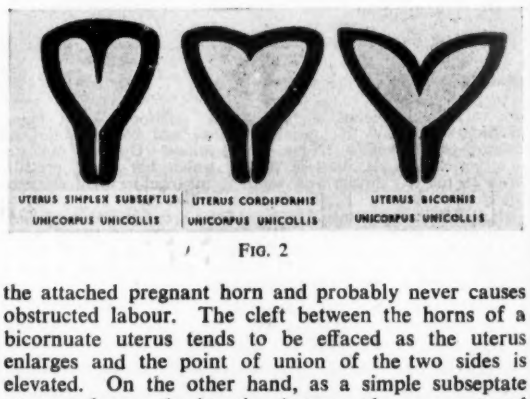
The simplest type of fusion deformity of the uterus is uterus arcuatus unicorpus unicollis, in which the uterine fundus is slightly depressed and its myometrial layer is thin, the uterine cavity is single and undistorted, and only one cervical canal is present (Fig. 1). In this type of uterus there is minimal disturbance of the normal progress of pregnancy and labour, and the deformity is frequently overlooked. However, the fundal depression may be slightly accentuated during the course of pregnancy, the fundus may appear slightly broader than usual, and the lie may be slightly oblique. Sometimes, especially when the breech presents, the fundal pole of the foetus may be felt with unaccustomed ease. The progress of the first and second stages of labour is usually normal, but the third stage may be prolonged, often owing to failure of separation of a fundal placenta. During manual detachment of such a placenta the impression may be gained that the fingers may tear through the exceptionally thin fundal myometrium.



UTERUS ARCUATUS
UNICORPUS UNICOLLIS

FIG. 1

Uterus simplex subseptus unicorpus unicollis, uterus cordiformis unicorpus unicollis, and uterus bicornis unicorpus unicollis all have in common a single bilobed uterine cavity and a single cervical canal (Fig. 2). As the ovum may be confined in a relatively indistensible recess near a uterine cornu, where it may possibly be implanted upon a less vascular area on the medial uterine wall or septum, abortion often occurs. There may also be an increased incidence of hyperemesis, toxaemia, and accidental ante-partum haemorrhage, but this is difficult to confirm. As pregnancy progresses, the hypertrophied non-pregnant horn is invariably lifted from the pelvis by the attached pregnant horn and probably never causes obstructed labour. The cleft between the horns of a bicornuate uterus tends to be effaced as the uterus enlarges and the point of union of the two sides is elevated. On the other hand, as a simple subseptate uterus enlarges, the junction between the pregnant and non-pregnant horn becomes more apparent.



UTERUS SIMPLEX SUBSEPTUS UNICORPUS UNICOLLIS | UTERUS CORDIFORMIS UNICORPUS UNICOLLIS | UTERUS BICORNIS UNICORPUS UNICOLLIS

FIG. 2

The lie of the foetus is usually longitudinal or oblique with the vertex or breech presenting, but the incidence of transverse lie is high. In longitudinal lie the presenting part usually expands the lower segment and approximates to the cervix in a normal manner. In vertex presentation the breech, and in breech presentation the vertex, may occupy one cornu, and the feet, possibly with the placenta, may occupy the other. About 12% of all cases of transverse lie are associated with these types of uterine deformity, and the convex foetal back and shoulder usually occupy the concavity of the lower segment. Hypotonic inertia and incoordinate uterine action, with consequent prolongation of the first and second stages of labour, are of more frequent occurrence, even with a longitudinal lie, but the incidence

*Read at a meeting of the Swedish Gynaecological Society held in Stockholm on May 25, 1960.

is not nearly so high as in cases of double uterus (uterus bicorpus). In association with transverse lie premature rupture of the membranes, prolapse of the cord, premature labour, abnormal uterine action, and obstructed labour may occur. In all cases the placenta is more liable to be retained, atonic post-partum haemorrhage is fairly frequent, and lochia may be excessive or prolonged in the puerperium.

Double Uterine Cavity

In uterus simplex septus bicorpus and uterus bicornis bicorpus—unicollis or bicollis—the uterine cavity is completely divided at least as far as the internal cervical os. Two separate compartments which do not communicate with one another are formed and the uterus is therefore a true double uterus (Fig. 3). Loculation of

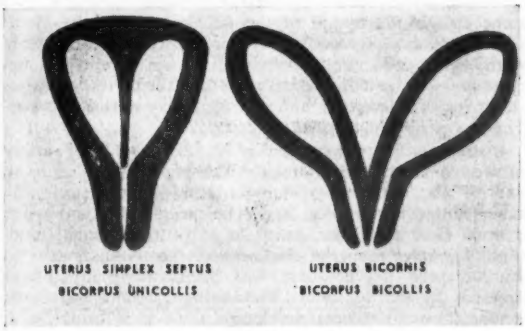


FIG. 3

the ovum results in a high rate of abortion and premature labour. There may be a high incidence of hyperemesis and toxaemia, although my personal findings on these points have been inconclusive. Bleeding may occur, especially during the early months of pregnancy, from the non-pregnant horn; but this does not occur in the majority of cases, and the amount of loss is usually small. Accidental ante-partum haemorrhage is apparently more frequent than in normal cases. The non-pregnant horn of the bicornuate uterus cleft externally to the level of the internal cervical os is liable to rotate into and become impacted in the pouch of Douglas, where it may subsequently cause obstructed labour. If the uterine cleft does not reach the internal os it will nearly always be raised during pregnancy, or occasionally during labour, above the level of the pelvic brim and will not then be apt to obstruct labour. The foetal lie is almost invariably longitudinal, but the incomplete breech commonly occupies the fusiform lower segment and constitutes the presenting part. Twin pregnancy is commoner in double than in single uteri.

The lower uterine segment may resist expansion in late pregnancy and during labour. This may lead to non-engagement of the presenting part in the pelvis and failure of approximation of the presenting part to the cervix. Incoordinate uterine action or hypotonic inertia with subsequent prolonged labour, and possibly arrest of progress and foetal and maternal distress, is particularly apt to arise. If labour is obstructed by the non-pregnant uterine horn uterine rupture may occur, especially through the scar of a previous caesarean section or the thin medial wall of a bicornuate uterus. A cervical or vaginal septum may obstruct labour or may, on being lacerated during the birth, bleed profusely. On occasion the presence of a recto-vesical septum may add to the difficulties of caesarean section (Hunter, 1960). Retention of the placenta and atonic post-partum haemorrhage, which may be severe, often occur. On rare occasions, when manually removing a retained placenta from a septate uterus, the oedematous, bruised, and possibly lacerated uterine septum may be mistaken for a subendometrial fibromyoma. Loss of blood during the puerperium may be excessive and prolonged, and the decidua of the non-pregnant horn may be discharged piecemeal or as a complete cast towards the end of the first week after delivery.

Summary

Although in the majority of cases of uterine deformity pregnancy and labour are normal, the incidence of complications is much higher than would be expected if the uterus was normal. If the risks are known and anticipated, earlier recognition and prompt treatment will undoubtedly reduce the hazards of pregnancy and labour.

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IDIOPATHIC CARDIOMEGALY

BY

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"Heart muscle," says Cameron (1952), "hypertrophies for many causes, all of which increase the amount of work thrown on the muscle." This conception of hypertrophy involves an increase in the mass of each muscle cell, without an increase in the total number of muscle cells. It also limits the conception to an increase brought about by a work stimulus such as, for example, valvular disease or increased peripheral resistance from hypertension. So far as we are aware, the steps by which work stimulus is translated to increase in cell mass await elucidation. In the meantime it becomes increasingly clear, as more and more cases are reported, that not all abnormal increases in total muscle mass are due to work stimulus. A group of cases variously described as idiopathic hypertrophy, familial cardiomegaly, asymmetrical hypertrophy in young adults, or hypertrophy of unknown aetiology have in common the absence of a work stimulus to account for the increase in muscle mass.

The two cases here reported illustrate the condition of the heart in the latter category. Both cases came to necropsy at the instance of the coroner. Commonly, in coroners' cases there is little or nothing in the way of clinical history to aid the pathologist in diagnosis. If he is confronted by a case of sudden death in which the sole finding is a heart with an obviously hypertrophied left ventricle showing marked excess of weight over the average for the sex, age, and development, the tendency is to attribute death to hypertensive heart

failure unless there is some special feature, such as its occurrence in a child or young adult or an obvious explanation for the hypertrophy. In the second case here reported, which occurred in a middle-aged man, probably such a cause of death would have been declared, but for the fact that hypertension was denied by the clinical history. We feel, therefore, that this condition may be commoner in older age-groups than is generally appreciated.

Case 1

The deceased was a youth of 16 who worked as a clerk. He had never had any serious illness. The only recent medical attention he had had was six weeks before his death, when he had an attack of influenza, from which he appeared to have fully recovered. On the afternoon of his death, he had gone for a ride on his cycle—one of his usual activities—when he was seen to fall off for no apparent reason. A near-by policeman, who was summoned, stated that he found the youth in a coma, breathing very deeply, with purple cheeks, lips, and ears. He died while being conveyed to hospital.

Necropsy Findings

The body was that of a tall youth of normal physique. There were some trivial injuries, sustained by his fall, of no significance as regards the cause of death. There was froth in the trachea. The pleura and lungs appeared healthy. The heart weighed 550 g. It was grossly hypertrophied on the left side, and the cavity of the left ventricle was dilated. The valves were healthy. There was no congenital defect in the heart, its valves, or vessels, and there was no congenital narrowing of the aorta. The muscle of the left ventricle was pale The papillary muscles were abnormally thick. The left coronary ostium was smaller in diameter than the right, and opened into a main trunk, which divided almost immediately into descending and transverse branches. The latter was very small, and indeed served only a negligible fraction of the usual field of supply of this branch. The descending branch also appeared small, and certainly so in relation to the large muscle mass, which lay in its field of supply. The lumen of the right artery was larger than that of the left and carried a blood supply to most of the area usually serviced by the transverse branch of the left artery. No atheroma was noted in the coronary arteries. There were no other findings of note except some congestion of the abdominal viscera.

Histological Findings

The heart muscle presented an appearance of bizarre dishevelment (Fig. 1). The fibres were coarse and at many points showed loose ends, as if broken across. Small foci of necrosis were present throughout the muscle. Here and there the muscle was replaced by collagen of loose texture, infiltrated in some cases diffusely with a small number of lymphocytes. Generally there was increased cellularity of the interstitial tissue. The muscle fibres generally were two or three times as thick as is seen in sections of normal heart. The fibrils were discernible as entities, separated by clear spaces, and in both longitudinal and transverse sections there were numerous large clear vacuolar spaces within the fibre (Fig. 2). Many of the nuclei were enlarged to about four times normal size. Many were hyperchromatic, in many the chromatin was finely granular, and some showed disruption of the nuclear membrane. Occasional twin nuclei were to be seen. At the poles of the nuclei were moderate collections of yellowish-brown pigment granules, usually described as lipofuscin. Appropriate stains for fats, amyloid, and glycogen gave negative results. There was no endocardial fibrosis.

Microscopical examination of the left coronary artery showed appreciable subintimal thickening of the main trunk and of the descending branch during its course in the subepicardial tissue (Fig. 3). The intimal thickening was entirely fibrous in character. In parts it was equal to or slightly greater than the thickness of the muscularis. No atheromatous degeneration was seen. In many places opposite to the subintimal thickening the internal elastic lamina showed degenerative change.

Case 2

The deceased was a colliery worker, aged 57, who, until seven years before his death, had been engaged in heavy work at the coal-face, and was in good health. At that time he noticed swelling of the ankles, and experienced discomfort in the right hypochondrium, and breathlessness. He thereupon consulted his doctor, who found oedema of the ankles and feet, an enlarged and tender liver, raised venous pressure, cyanosis, and irregular pulse and heart

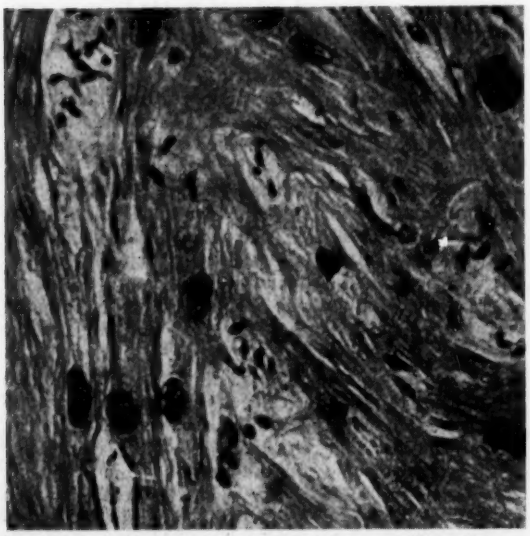

Fig. 1.—Case 1. Heart muscle, showing coarse dishevelled appearance with grossly thickened fibres, separation of fibrils, giant hyperchromatic nuclei, and increased cellularity of interstitial tissue. (Haematoxylin and eosin. ×240.)

Fig. 2.—Case 1. Transverse section of heart muscle, showing clear vacuolar spaces within the fibres. (Masson's trichrome. ×240.)

sounds, the rate being uncountable. His doctor found no evidence of mitral disease, hypertension, or thyrotoxicosis. He treated the patient with digitalis for five weeks, with a response which he assessed as fair, and then referred him to hospital, where on examination there was no evidence of congestive failure.

His heart appeared to be of normal size. Blood-pressure was 150/78. There was atrial fibrillation at a rate varying during his stay in hospital from 100 to 124 a minute. The electrocardiogram showed also some ventricular extrasystoles with flattening of T waves. It was thought that the findings indicated coronary ischaemia. There was no suggestion of a recent coronary occlusion. There were no heart murmurs; but numerous widely scattered skin petechiae (which the patient said came and went intermittently) and a palpable spleen prompted an investigation for bacterial endocarditis. He had no rise in temperature during his stay in hospital, and five successive blood cultures were negative for organisms. His haemoglobin level was 14.8 g./100 ml., and the red blood count 5,100,000/c.mm. Sedimentation rate was normal. White blood count totalled 9,500/c.mm., with normal differential. Radioiodine tests disclosed results consistent with normal thyroid function in all respects.

On discharge the spleen had receded in size. His heart was still fibrillating at an uncontrolled rate, but he appeared reasonably well. He was kept on digitalis and was under regular medical supervision until his death. He resumed work as a conveyer-belt attendant, which involved merely the control of switches. Thus he continued with an occasional short absence from work, and with no substantial change in his condition. At no time did his doctor find any rise in his blood-pressure. On October 29, 1958, he was found dead while at work. He had been seen about an hour before, apparently well and cheerful.

Necropsy Findings

The body was that of a well-nourished middle-aged man. The main findings related to the heart, which weighed 675 g. It was dilated and hypertrophied on both sides, but particularly on the left. There was no congenital defect in the heart, its valves, or its vessels. The heart valves were normal. There was some narrowing of the coronary arteries, but this was assessed as mild. There was no occlusion. The heart muscle appeared healthy, and no fibrosis was evident. All the peripheral vessels were healthy, and showed no congenital defect. In particular, there was no coarctation of the aorta. There was congestion of the spleen, and the liver was rather fibrous.

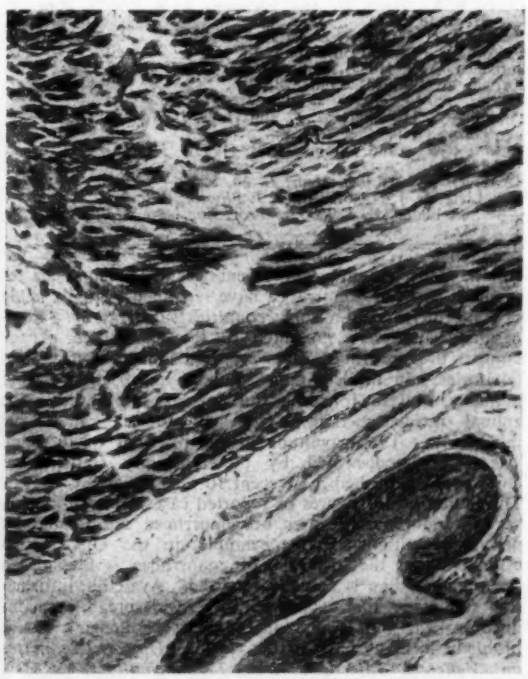

FIG. 3.—Case 1. Coronary artery, showing subintimal thickening. The adjacent muscle shows the appearance of breakage of the fibres. (Masson's trichrome. ×60.)

Histological Findings

The main findings related to the heart. The changes were substantially the same as those in Case 1, though in this heart the patches of collagen replacement of muscle were generally larger, more condensed, and more numerous than in Case 1. Apart from the changes in the heart, the lungs showed slight thickening and increased cellularity of the alveolar septa. There was some alveolar oedema. The arteriolar walls were slightly thickened. The liver was congested and oedematous. There was slight fibrosis of the portal tracts, and a mild fibrotic change surrounding the central veins of the lobules. The sinuses of the splenic pulp were greatly distended and literally stuffed with red cells. The lining cells of the sinusoids were clearly picked out by reason of their heavy uptake of iron-containing pigment. The smaller vessels of the kidneys were markedly congested, and the pyramidal interstitial tissue was oedematous. There was no arterial or arteriolar thickening in the kidneys. The thyroid gland was normal.

Discussion

The two cases reported belong to a group which is coming to be recognized as one with a characteristic clinical and pathological pattern. As happens when an entity is in process of recognition, there is often dispute and confusion concerning its truly fundamental features. It appears to us that the fundamental features of this group are a marked increase in cardiac muscle mass, an absence of any work stimulus to account for this increase, and a marked liability to sudden death from heart failure. The cause or causes have so far not been defined, though, as is usual in any so-called "idiopathic" entity, there is no lack of suggestion regarding possible causes. Among the commoner causes canvassed have been vitamin deficiency (notably of the B complex), potassium deficiency, strenuous exercise, arrythmias, anoxia, coronary arteriosclerosis, thyrotoxic heart disease, specific and non-specific myocarditis, subendocardial fibrosis, von Giercke's disease, and amyloid disease. With the exception of anoxia, all of these causes have been excluded from many undoubted cases of this entity, and we agree with Elster *et al.* (1955) that there is little point in reciting a list of suggested causes without any adequate evidence to support their claim.

The question whether deficiency of oxygen to the heart muscle can produce increase in myocardial mass has been debated in the literature. Experimental work in animals and observations on human beings exposed to high altitudes have been held to negative such a hypothesis. However, Serbin and Chojnacki (1955) have suggested (we think rightly) that the exposures in these cases to deficiency of oxygen were too short for a valid conclusion to be drawn. A wide spectrum of oxygen deficiency, both quantitative and as regards duration, can be envisaged in the human. The needs of the heart vary widely with the patterns of activity. There are compensatory mechanisms such as polycythaemia, whose limits we do not know. All of these

features combine to make the dynamic picture so complicated that it is difficult to conceive the possibility of designing suitable experimental conditions.

We think there is clear evidence in human pathology for the thesis that increase in cardiac muscle mass results from anoxia. When the coronary arteries originate in the pulmonary artery the myocardium inevitably suffers from anoxia over a long period. Jurishica (1957), in reviewing 12 adult cases of this anomaly in the left coronary artery, showed that increase in the mass of the left ventricle and liability to sudden death from heart failure were characteristic. Indeed, no one can read the reports of cases of this anomaly without being struck by the similarity of the clinicopathological features to those in so-called idiopathic hypertrophy. Again, it would appear to be clearly established that chronic anaemia causes increase in myocardial mass (Paplanus *et al.*, 1958), and chronic exposure to high altitude has been found to produce increase in cardiac muscle mass (Van Liere, 1936; Kerwin, 1944; Van Liere *et al.*, 1955). The common factor in all of these induced increases in muscle mass is chronic deficiency of oxygen.

In our view the thesis that chronic oxygen deficiency to the heart muscle is the fundamental cause of the clinicopathological entity under discussion is by far the most convincing. Inevitably, this raises the question of coronary insufficiency in these cases. It must be admitted that in many of the cases no mention is made of any defect in the coronary blood supply, but we do not think that is surprising. The assessment of the sufficiency of the coronary blood supply is, in practice, at best a crude one, and we doubt whether it normally involves more than a naked-eye inspection of parts of the coronary vessels by the pathologist. It appears to us that a much more detailed examination of the coronary vessels is required for a valid assessment, and some such injection and radiographic technique as was carried out by Fulton (1956) is called for, particularly in cases where the insufficiency is not concentrated in the major branches of the coronary arterial tree. Weight is lent to the theory of chronic anoxia and coronary insufficiency by the persistent reports of anomalies or defects in the coronary circulation in cases of unexplained cardiomegaly.

In our second case the naked-eye assessment of the coronary arteries was that they were narrow, the degree of narrowing being assessed as mild. Unfortunately only small portions of the heart muscle were retained for histology in this case. In Case 1 the naked-eye investigation of the coronary tree suggested insufficiency, and this was reinforced by the finding of extensive intimal fibrosis of the descending branch of the left artery on microscopy. Small coronary arteries as compared with the grossly hypertrophied ventricles have been noted before (Campbell and Turner-Warwick, 1956; Evans, 1957). Case 1 described by Fulton (1956) was one of cardiomegaly in which hypertension or other work stimulus was ruled out, and the other finding was pronounced coronary atheroma with narrowing. Master (1954), in a study of 600 cases of coronary artery disease, found that increase in cardiac muscle mass occurred "simply and definitely in the presence of coronary sclerosis alone." He held the cause to be obscure, but pointed out that in arteriosclerosis of these arteries there is anoxaemia of the myocardium. We agree with Campbell (1960) that there is too much tendency to say, when you find a large heart, that there must have been hypertension in the past.

Many of the reports make a feature of the familial character of the unexplained cardiomegaly with the implication that there is some inherited defect intrinsic to the cardiac muscle. It is quite feasible that the familial incidence noted in a number of the reports of this condition may be due to the inheritance of anomalies in the coronary tree, which produce coronary insufficiency and anoxia. The asymmetrical character of the cardiomegaly noted by Teare (1958) is consistent with the theory of anoxic cardiomegaly. It is only to be expected that, if anoxia is produced by mechanical insufficiency of the coronary arteries, then in many cases the condition would have a distribution in the local field of supply of branches of the arterial tree.

Summary

Two cases of cardiomegaly, not due to work stimulus, are described. It is suggested that, since it is clear that cardiomegaly can be a result of chronic deficiency of oxygen, a much more careful assessment of the sufficiency of the coronary blood supply should be carried out in cases of unexplained cardiomegaly than is usual in present pathological practice.

Our thanks are due to Dr. A. W. D. Leishman for permission to publish the clinical details of Case 2. We are grateful to Mr. A. P. Lockwood, H.M. Coroner for the City of Sheffield and for the Rotherham Division of the West Riding of Yorkshire, for permission to publish the details of both cases. For technical assistance and the preparation of the illustrations we are indebted to Mr. R. T. Clegg.

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"In many countries in recent years the numbers of reported cases of gonorrhoea have remained virtually static or have increased—in some countries substantially. Comparative data were presented to the Committee of the number of gonorrhoea cases reported in 22 countries and territories. In no less than 15 there has been a rise in numbers, and in four the situation appears static. The annual incidence ranges from 10 to 50 per 10,000 inhabitants. The magnitude of the reservoir of infection was also demonstrated by the morbidity statistics of gonorrhoea published in a recent 10-year review by W.H.O. The limitations of figures of reported cases are well known, as many unreported cases of gonorrhoea are treated by private practitioners. For example, in the U.S.A. it is estimated that the incidence of gonorrhoea is five to ten times higher than is actually reported. Available information indicates that gonorrhoea is widespread, remains uncontrolled, and is one of the most challenging health problems in many parts of the world." (*Expert Committee on Venereal Infections and Treponematoses*, W.H.O. Technical Report Series, No. 190. Available from H.M.S.O., P.O. Box 569, London S.E.1, price 5s.)

DEXAMETHASONE MYOPATHY

BY

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AND

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The complications of muscular weakness and wasting have been observed since the earliest days of adrenal corticosteroid therapy. Ellis (1956) studied muscular lesions in rabbits after repeated injections of cortisone. Widespread necrosis of muscle occurred, and the changes were similar to those found in muscular dystrophy and dermatomyositis. Perkoff *et al.* (1959) reported severe weakness and muscular atrophy in seven patients treated with cortisone over five years, and noted that the lower limbs were mainly affected. Harman (1959) quoted two cases of weakness of the legs which occurred after prednisone therapy.

More striking reports of wasting came with triamcinolone (9-alpha-fluoro, 16-alpha-hydroxyprednisolone) therapy. It was noted by Dubois (1958) while treating three patients suffering from systemic lupus erythematosus with this steroid, the extensors of the legs and deep muscles of the back being chiefly affected. After the patient was transferred to hydrocortisone or prednisone, the muscles gradually returned to normal. Kendall and Hart (1959) observed a loss of weight of over 14 lb. (6.4 kg.) in five patients receiving triamcinolone, and in four of these rapid symmetrical muscle-wasting occurred. R. S. Williams (1959) described three cases in which weakness occurred in the trunk and in the pelvic and shoulder muscles, and likened the syndrome to the muscular dystrophies and to the myopathies complicating thyrotoxicosis and carcinoma.

MacLean and Schurr (1959) reported a case in which muscular atrophy complicated treatment with fludrocortisone (9-alpha-fluorohydrocortisone) and suggested that the presence of a fluorine atom in the 9-alpha position of the steroid nucleus might render this complication more likely. Thompson (1959) stated that, should this in fact be so, the newest steroid, dexamethasone (9-alpha-fluoro, 16-alpha-methylprednisolone) might in turn be capable of producing this effect.

Boland (1958, 1959) indicated that the incidence of side-effects from dexamethasone was the same as from prednisolone when equally effective antirheumatic doses were given, and did not observe weight-loss or weakness. There have been, in fact, some reports of muscular weakness with dexamethasone: G. T. Williams (1959) treated 16 patients with triamcinolone and then dexamethasone, and one had to discontinue steroid therapy because of general weakness and muscular pains. Duvenci *et al.* (1959) gave dexamethasone to 41 patients with bronchial asthma, and muscular weakness occurred in two of these. Walton (1959) observed a similar incidence of weakness in 52 patients treated for allergic disorders. However, in none of these accounts has definite myopathy been noted.

Kendall recently has observed myopathic lesions in dexamethasone-treated rats (personal communication).

The purpose of the paper is to report an example of severe myopathy, apparently attributable to dexamethasone, in a patient with bronchial asthma.

Case Report

A 59-year-old man had suffered from recurrent attacks of bronchial asthma for 30 years. He was treated with prednisone in a dosage of 30 mg. daily for eight weeks (starting October 8, 1959) with temporary improvement, and then with dexamethasone (2.25 mg. daily), which resulted in a further clinical remission. A month later he developed septic lesions in the hands which necessitated surgical incision of the proximal pulp spaces and subsequently amputation of the fifth finger of the right hand. Dexamethasone therapy was continued throughout, and on February 16, 1960, he was referred to the physical medicine department with a complaint of weakness, pains in the thighs, and in particular difficulty in mounting stairs.

FIG. 1.—Showing quadriceps wasting, abdominal bloating, and mooning of face.

On examination he was obese and the abdomen was greatly distended. The lower limbs were by contrast thin and there was considerable symmetrical wasting of both quadriceps muscles (Fig. 1). The deep reflexes were brisk, the muscles of the arms and trunk were of normal power, and there were no sensory disturbances. There was moderate facial mooning. The blood-pressure was 160/90.

The patient was admitted to the Royal Victoria Infirmary on March 12, 1960, for observation.

Investigations

Radiograph of pelvis, normal. Haemoglobin, 110% (16.3 g./100 ml.). Serum electrolytes: Na 138, K 3.1, Cl 96 mEq/l. Serum calcium, 10.4 mg./100 ml. Liver function tests, within normal limits. Urinary creatine excretion, 615 mg. in 24 hours (normal, 25 mg. in 24 hours). Urinary creatinine excretion, 924 mg. in 24 hours (normal, 100 mg. in 24 hours). Serum aldolase, 8 units (Bruns)

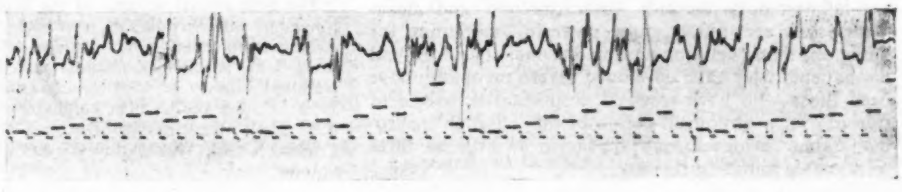

FIG. 2.—Electromyogram: motor unit potentials on volition, with frequency analysis histogram, showing shift to right. Calibration at 50 cycles and 100 microvolts.

(normal, 3 to 9 units). Muscle biopsy, no histological abnormality found in excised portion of right quadriceps muscle.

Electrodiagnosis

Electromyograms from the right quadriceps muscle were recorded. There was no spontaneous activity, but on volition a full interference pattern of lower-than-normal amplitude was obtained. The pattern was made up of a great many polyphasic and short-duration potentials. The appearances were diagnostic of a myopathic disorder (Fig. 2).

Progress

On March 25, 1960, dexamethasone was discontinued and prednisone and norethandrolone were started. A few days later the patient noticed symptomatic improvement. He was able to walk round the ward without discomfort, and he returned home on April 2, 1960.

By May 4, 1960, he claimed a considerable return of power. A further electromyogram next day again showed a number of myopathic potentials, but the volitional pattern from much of the muscle was normal, and it seemed clear that the myopathic changes were less striking than previously. However, the 24-hour urinary output of creatine has remained high (1,002 mg. on May 6, 1960).

Discussion

In the present case electromyographic evidence of myopathy was unequivocal, and it may be concluded that bilateral quadriceps wasting was induced by dexamethasone given in a dosage of 2.25 mg. daily over a period of 11 weeks.

The cause of "steroid myopathy" is not yet clear. It is probable that the disorder is one of muscle metabolism, and that the structural changes, if any, are secondary. In this case a random biopsy of one of the quadriceps muscles showed nothing abnormal. Prolonged administration of dexamethasone in doses of 10 mg. or more produces an increase in nitrogen excretion, which is reversed on withdrawal of the drug (Bunim *et al.*, 1958). This may account for the disorder, but triamcinolone produces a similar myopathy and has no greater katabolic activity than prednisolone (R. S. Williams, 1959). Evidence of muscle breakdown is presented by creatinuria, which was marked in this case. The serum aldolase was normal, but it has been found to be raised in only a minority of cases of myopathic disorders (Evans and Baker, 1957).

It is generally agreed that muscular wasting can be due to any of the anti-inflammatory steroids that have been used in clinical practice, but the more severe instances with electromyographic evidence of myopathy have been reported with fludrocortisone, triamcinolone, and now dexamethasone. It thus seems that, in common with many other side-effects known to occur with steroids, this complication will occur particularly with some steroids, and to a certain extent with others, but the pattern of the incidence and severity is not identical. The balance of evidence at present suggests that myopathy complicating steroid therapy probably does occur more often in those patients receiving steroids containing the 9-alpha-fluorine configuration. However, it is to be borne in mind that the newer halogenated anti-inflammatory steroids (triamcinolone and dexamethasone) are much more powerful milligram for milligram than cortisone and prednisone, and in general the patients who have developed severe myopathy have been those who have received a substantial dosage of steroid over a prolonged period of time, though electromyographic evidence may appear in as little as three weeks after initiating therapy.

Abdominal distension, often termed "bloating," occurs quite often in patients treated with dexamethasone, and gradually decreases when the steroid is withdrawn (Boland, 1958).

Summary

Bilateral quadriceps-wasting followed dexamethasone therapy in a patient with bronchial asthma. There were electromyographic changes of myopathy as previously described with triamcinolone and fludrocortisone.

The muscle weakness and electromyographic changes are resolving since substitution of prednisone for dexamethasone.

The cause of "steroid myopathy" is unknown, but its occurrence during dexamethasone therapy seems to substantiate previous hypotheses that the myopathy may be especially associated with those adrenal steroids which contain a fluorine atom in the 9-alpha position of the nucleus.

Addendum.—Since the above report was written we have observed myopathic changes in a 52-year-old man with rheumatoid arthritis of seven years' duration, who had been receiving dexamethasone for 15 months. He was given prednisolone, 10 mg. daily, from October, 1957, until May, 1959, and subsequently had dexamethasone in a dosage of 2 mg. daily. Within a few months he gained weight and developed slight oedema of the legs and characteristic abdominal "bloating." In May, 1960, 12 months after starting dexamethasone therapy, he complained of increasing weakness in both thighs. Serial electromyograms on the quadriceps muscles have shown a reduced interference-pattern with increasing preponderance of short-duration potentials indicative of a myopathy.

Although in this instance it is possible that the electromyographic pattern demonstrates a myositic process which may occur in some patients with long-standing rheumatoid arthritis, the occurrence of progressive myopathic changes in the large proximal muscles and their association with other typical side-effects of dexamethasone strongly suggest that they are, in fact, consequent upon dexamethasone therapy.

We wish to thank Dr. A. G. Ogilvie, under whose care the patient was admitted, for permission to report this case, and Dr. M. Thompson for his advice.

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SERUM TRANSAMINASE ACTIVITY IN DISSECTING ANEURYSM OF THE AORTA

BY

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Although many reports have appeared in the literature about the clinical significance of elevated serum transaminase activity, little has been written of transaminase activity, in dissecting aneurysm of the aorta. Agress (1959) in a detailed, critical evaluation of the transaminase test does not mention its usefulness in the diagnosis of this disorder. We have found only five cases of aortic dissection in the literature in which serum transaminase estimations were performed (Kattus *et al.*, 1956; Meenan, 1957; Tredway and Kemble, 1958). We have recently had under our care three patients with dissecting aneurysm of the aorta in whom serial transaminase activities were estimated.

Case 1

This patient, a man aged 52, had been well until seven days before admission, when, while at work, he suddenly experienced a constricting retrosternal pain which radiated to the jaws, arms, back, and groins. From that time until admission the pain persisted; he had felt continually faint, cold, and clammy, and had noticed that his urinary output had diminished.

On examination he was shocked, cold, clammy, and cyanosed; pulse 120/minute and regular; B.P. 110/70 mm. Hg; heart sounds—apical triple rhythm. Femoral and all peripheral pulses were present and equal. The liver was tender and palpable two fingerbreadths below the right costal margin. There was slight ankle oedema but no rise in J.V.P.

Investigations.—Haemoglobin, 113%; W.B.C., 8,700; E.S.R., 24 mm./hour (Westergren); urea, 66 mg./100 ml.; serum amylase, 260 units; serum total protein, 5.5 g./100 ml. (albumin 3.5 g.); serum alkaline phosphatase, 13.8 King–Armstrong units/100 ml.; thymol turbidity, 1 unit; zinc turbidity, 3 units. Portable *x*-ray examination of the chest revealed a small left pleural effusion. E.C.G. showed changes suggestive of an old posterior myocardial infarction. Serum transaminase activity was as shown in Table I.

TABLE I.—*Transaminase Activities in Case* 1

Day of Illness:	7	8	9	10	11	12	13	14
S.G.O.T. ..	480		1,300			70	65	60
S.G.P.T. ..			1,300	1,100		80	300	200

Progress.—He had persistent oliguria (maximum urinary output 370 ml. in 24 hours) and rapidly developed renal failure (urea 340 mg. on eighth day). He was treated with restricted fluid intake, 40% dextrose, and hydrocortisone, erythromycin, oxytetracycline, and codein. co. orally (8 gr. (0.5 g.) throughout the admission). He died on the ninth day.

Necropsy.—There was a dissecting aneurysm of the aorta extending from the aortic valve cusps to the bifurcation, and a large subepicardial haemorrhage due to backward extension of the dissection. There was a healed infarct in the posterior wall of the left ventricle. No recent myocardial infarction was present. Histologically the liver showed hepatic congestion with fatty change, and the kidneys showed tubular necrosis.

Case 2

This man, aged 56, had been treated for essential hypertension for the past five years. Over this period he had received pentolinium, pempidine tartrate, and hydrochlorothiazide with good effect. He was well until the day of admission, when he suddenly developed retrosternal pain, which radiated into the back and lasted for two hours. Later on the pain returned more severely and was accompanied by sweating and faintness.

On examination he looked ill but was not shocked; pulse 108/minute and regular; B.P. 243/160 mm. Hg; heart sounds—apical triple rhythm. The femoral pulses were unequal, the right being of larger volume than the left.

Investigations.—Haemoglobin, 103% (15.2 g./100 ml.); W.B.C., 15,000; E.S.R., 8 mm. fall in 1 hour (Westergren); urea, 47 mg./100 ml.; E.C.G. showed ischaemic changes but no recent infarction. Serum transaminase activities are shown in Table II. Serum amylase, 120 units/100 ml.

TABLE II.—*Transaminase Activities in Cases* 2 *and* 3

Day of Illness:		1	2	3	4	5	6	7
Case 2	S.G.O.T. ..	14	16		15	23	27	
	S.G.P.T. ..						29	
„ 3	S.G.O.T. ..	15	15	14				
	S.G.P.T. ..	7	9	7				

Progress.—A diagnosis of dissecting aneurysm was made and conservative treatment with hypotensive agents was instituted. He became pain-free after 48 hours but continued to experience occasional episodes of backache throughout the admission. He died suddenly on the 17th day.

Necropsy.—There was a dissecting aneurysm of the aorta from the level of the origin of the left subclavian artery to the bifurcation. The aneurysm had ruptured into the left pleural cavity. There were ischaemic changes in the left ventricle but no evidence of recent or previous infarction.

Case 3

For the past 18 months this patient, a man aged 47, had been treated for essential hypertension with reserpine. He had remained well until the day of admission; then, while at work, he suddenly experienced lower back pain which radiated around the costal margin, down to the thighs and upwards into the neck. The pain became progressively worse, and after four hours he began to feel ill and faint.

On examination he looked ill but not shocked; pulse 80/minute and regular; B.P. 170/90 mm. Hg; heart sounds normal. The right femoral pulse was of smaller volume than the left.

Investigations.—Haemoglobin, 98% (14.1 g./100 ml.); W.B.C., 12,800; urea, 29 mg./100 ml.; serum amylase, 265 units/100 ml. Chest *x*-ray examination showed nothing abnormal. E.C.G. showed no evidence of recent myocardial infarction. Serum transaminase activities are shown in Table II.

Progress.—The patient continued to experience pain in the back for the next five days, although his general condition remained unchanged. A diagnosis of dissecting aneurysm was made and a laparotomy performed (Mr. L. P. Thomas). At operation the aorta was found to be the seat of a dissecting aneurysm extending from above the diaphragm to the bifurcation. A re-entry ostium was made in the abdominal aorta. He made a good recovery and was still alive and well at the time of writing.

Discussion

Clinically dissecting aneurysm of the aorta may mimic myocardial infarction, and with the discovery that serum glutamic oxalo-acetic transaminase (S.G.O.T.) was increased after the latter (LaDue *et al.*, 1954) it was suggested that this test might be of value in differentiating

the two conditions (Sampson, 1958). Reviewing this problem, Tredway and Kemble (1958) reported three cases of dissecting aneurysm of the aorta, in two of which elevated S.G.O.T. activity was found. In these two cases the maximum level of S.G.O.T. was 115 and 135 units, and this they attributed to pericardial haemorrhage due to extension of the dissection into the pericardial sac. They concluded that the test was not of very great value as an aid to the diagnosis of this disorder. In the remaining three cases reported in the literature normal values of S.G.O.T. were found. This differentiation can be of considerable importance, as the treatment of the two conditions differs, and surgical operations are now being successfully performed for the relief of aortic dissections. However, surgery is contraindicated in cases with cardiac tamponade and established anuria (Rob and Kenyon, 1960).

In only one of the cases described above (Case 1) were high values for both S.G.O.T. and serum glutamic pyruvic transaminase (S.G.P.T.) activities found. Several mechanisms could have accounted for this rise:

1. Myocardial necrosis consequent upon subepicardial haemorrhage due to extension of the dissecting aneurysm.

2. Acute congestion of the liver.—Apart from primary hepatic disorders, high values of S.G.O.T. activity (700 to 3,000 units) have been recorded in cases exhibiting acute congestion of the liver due to acute heart failure (Shields and Shannon, 1958). In Case 1 there was both clinical and post-mortem evidence of acute hepatic congestion, and we believe that this was a major factor in the production of the high S.G.O.T. and S.G.P.T. activities recorded.

3. Codeine therapy and renal failure.—Although little is known of transaminase excretion it is thought that the role of the kidney in this process is a small one, as only minute quantities of the enzymes have been found in the urine of normal subjects. This view would appear to be supported by the finding of a normal S.G.O.T. activity (18 units) in a case of anuria reported by Chinsky *et al.* (1956) and in a case of obstructive anuria we have recently observed with values of 6 units (S.G.O.T.) and 1 unit (S.G.P.T.). It has been previously suggested that codeine causes a rise in S.G.O.T. and S.G.P.T. activity (Foulk and Fleisher, 1957). Case 1 received small doses of codein. co. orally, and this may have contributed to the raised S.G.O.T. and S.G.P.T. activities. Further retention of this drug in the body, as a result of acute renal failure, may have been an added factor.

Conclusion

It would appear that in dissecting aneurysm of the aorta there can arise factors such as heart failure, with acute hepatic congestion or extension of the aneurysm into the heart and pericardium, which could elevate the S.G.O.T. and S.G.P.T. activities. On the other hand, if the dissection has not produced these complications (as in Cases 2 and 3) normal serum transaminase activities would be expected. With these facts in mind we take the view that the transaminase test has a place in the diagnosis and management of dissecting aneurysm of the aorta.

We are indebted to Dr. William Phillips, under whose care these patients were admitted, for his helpful advice and criticism, and to Mr. L. P. Thomas for permission to publish the operative details.

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LATE RECURRENCE OF CARCINOMA OF BREAST

BY

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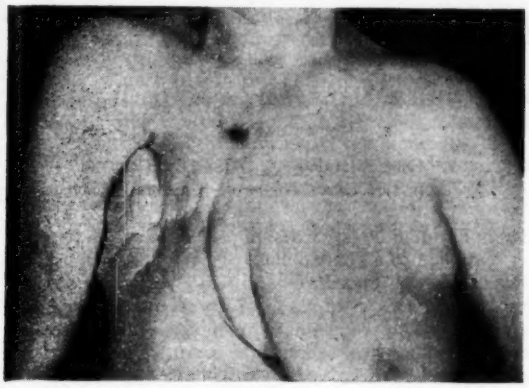
John Hunter (1837) observed that recurrence of carcinoma of the breast may occur many years after removal of the primary tumour. He stated that the recurrence "is either in the cicatrix, or in the lymphatic glands. The contamination extends in some instances on the inside of the sternum, in the course of the internal mammary artery. Sometimes these consequent cancers appear long after the operation, even years." In an earlier lecture he had stated, "I have seen instances where it was years after all continuance of the cause was removed before the glands in the armpit had taken on diseased action after contamination."

There have now been a number of cases reported in which a very long interval has elapsed between mastectomy and the first recurrence. They are of interest because they show that the term "cure" in cancer therapy must be used with reservation and emphasize the importance of lifelong follow-up of treated cancer patients.

The case reported here is one in which recurrence was first observed thirty-five years after radical mastectomy. There was recurrence in the scar and there were also multiple skeletal deposits.

Case Report

In 1925, at the age of 39, she presented at Hampstead General Hospital with a swelling in the right breast which had been present for two years. There were two hard nodes in the right axilla. Biopsy of the breast tumour showed spheroidal-cell carcinoma, and a right radical mastectomy was performed (Mr. Bryan). No histological report is available on the operation specimen. No radiotherapy was given. There was some sloughing of the operation flaps, and convalescence was slow. She stated that since the operation she had had a small red area at the upper end of the operation scar. It measured about 0.5 cm. in diameter and was flush with the skin surface. She had remained otherwise very well. In 1954 it developed a scab, and in 1958 it began to increase in size. About this time she noticed pain and weakness of the right arm. When she was seen at Hammersmith Hospital in 1960, at the age of 73, there was an ulcer at the upper end of the operation scar 2 cm. in diameter (see Fig.). The walls of the ulcer were red, raised, and hard. The floor contained a thick scab. There was a 2-cm. hard fixed node in the right supraclavicular fossa.



Showing recurrence of carcinoma of breast at upper end of operation scar.

Radiographs showed multiple metastatic deposits in the ribs, pelvis, thoracic spine, and right scapula. There were degenerative joint changes in the cervical spine which were considered to be the cause of her symptoms.

Biopsy of the ulcer showed infiltration of the dermis with malignant cells consistent with a metastasis from a primary carcinoma of the breast.

Discussion

There are a number of possible explanations here. This might be a new primary carcinoma arising in breast tissue that had been left behind at operation. This was thought unlikely, as no obvious breast tissue was present and the recurrence was actually on the operation scar. This might be a metastasis from a second primary carcinoma hidden in the opposite breast or in another part of the body, but there was no evidence of this on careful examination. The other possibility was that cancer cells had remained at the site of recurrence since operation, being dormant until 1958. This seemed to be the more likely explanation, especially as the patient stated that a small red spot had been present at the site of recurrence since the original operation. No illness or incident had occurred around the time that the lesion started to increase in size.

Fifty-eight cases with recurrence of breast cancer more than fifteen years after the initial operation have been collected from the literature and are presented in Table I.

As early as 1876 Boeckel reported a recurrence 29 years after mastectomy. The first cases in the British literature were published in 1887 by Bryant (recurrence after 25 years) and by Smith (recurrence after 19 years).

The longest period was reported in 1932 by Chauffard. He states that "several red violet nodules, doubtlessly cancer," appeared in the mastectomy scar 50 years after operation. The patient died of pneumonia several months later. No mention is made of histological or post mortem findings. Hartmann in 1942 described local recurrence after 46 years, but no details were given. Davidson and Ratcliffe (1946) published a detailed case report of a woman who had a bilateral mastectomy for bilateral breast cancer. This was followed 40 years later by metastatic deposits in the left supraclavicular lymph nodes. The patient died three years later. At necropsy there was no evidence of a new primary carcinoma and the lymph-node metastases were histologically compatible with breast carcinoma. Cade quotes a case in which first evidence of recurrence appeared as a parasternal deposit 40 years after radical mastectomy.

Table II shows the site of the first recurrence in this series. Of the 13 cases with distant metastases as the first recurrence, only five are reported to have had a post mortem examination by which a second primary carcinoma was excluded.

Post-operative radiotherapy was given to 4 cases out of the 58. One of these, however, had what to-day would be considered to be an inadequate dose. Many of the patients in this series had their mastectomy at a time when routine post-operative radiotherapy was not practised.

TABLE I.—*Reported Cases of Carcinoma of the Breast Which Have Had Their First Recurrence Fifteen or More Years After Mastectomy*

Recurrence (Years after Mastectomy)	Author	Date of Publication	Site of Recurrence ?=Not Stated	Histological Examination Primary/Secondary ?=Not Performed
50	Chauffard ..	1932	Mastectomy scar	?
46	Hartmann ..	1942	,, ,,	?
40	Davidson and Ratcliffe	1946	Lt. supraclavicular fossa	+/+
40	Cade	1950	Parasternal	?
35	Sutton	1960	Mastectomy scar and skeleton	+/+ spheroidal cell
34	Daland	1945	Mastectomy scar	?
32	Danckers *et al.* ..	1960	Parasternal	?/+ scirrhous
32	Lewis and Rienhoff	1932	Liver	?
31	Morton and Morton	1953	Skin of axilla	?/+
31	Bohlig	1955	Brain	?
31	Bowlby, cited by Gordon-Taylor	?	?	?
31	Steward, cited by Gordon-Taylor	1925	?	?
30	Gordon-Taylor ..	1939	Pelvis	?/+
30	Cade	1950	Parasternal	?
30	Heurtaux ..	1899	Mastectomy scar	?
30	Verneuil	1888	,, ? ,,	+/+ scirrhous
29	Boeckel	1870	?	?
27	Perry	1948	Pleura, mediastinum	+/?
25	Bade	1946	Lymph nodes of neck	?
25	Bryant	1887	Mastectomy scar	?
25	Matas, cited by Ransohoff	?	,, ,,	?
23	Gordon-Taylor ..	1939	,, ,,	?
23	Potherat	1909	Parasternal	+/+
22	Bade ..	1946	,,	?
22	Gordon-Taylor ..	1939	Mastectomy scar	?
22	Richard	1942	Humerus, same side	?/+
21	Gordon-Taylor ..	1939	Mastectomy scar	?
21	Haagensen ..	1956	Pleura, lung	+/+
21	Monod	1942	Axilla, same side	+/+
20	Bohlig (3 cases)	1955	?	?
20	Ransohoff ..	1907	?	?
20	Ficarra	1952	Generalized	?/+ adenocarcinoma
20	Haagensen ..	1956	Supraclavicular fossa, same side	+/+
20	Lewis and Rienhoff	1932	Mastectomy scar	?
20	Mitchell ..	1952	,, ,,	+/+ adenocarcinoma
20	Ransohoff ..	1907	Mastectomy	+/+ scirrhous
19	Bull, cited by Ransohoff	?	Generalized	?
19	Hartmann ..	1942	Vertebrae	?
19	,, ...	1942	Mediastinum	?
19	Josephy	1951	Contralateral axillary node	?/+
19	Smith	1887	Mastectomy scar	+/?
17	Coley, cited by Ransohoff	?	?	?
17	Gordon-Taylor (2 cases)	1939	Mastectomy scar	?
17	Powers	1910	,, ,,	+/+ scirrhous
17	Wawro	1954	Parasternal	+/+
16	Arnsperger ..	1905	Mastectomy scar	?
16	Gordon-Taylor ..	1939	,, ,,	?
16	Hartmann ..	1942	Parasternal	?
16	,, ...	1942	Ovary	?
16	Morton and Morton	1953	Axilla, skin of shoulder, same side	+/+
16	Nunn	1899	Mastectomy scar	?
16	Uffreduzzi ..	1930	?	+/+
15	Chilko and Quastler	1942	Mediastinum, pleura	+/+ medullary carcinoma
15	Huguenin and Gillet	1938	Mastectomy scar	+/+ scirrhous
15	Hartmann ..	1942	Lung	?

TABLE II.—*Site of First Recurrence in 58 Patients with Late Recurrent Breast Carcinoma*

Mastectomy scar		22 (38%)
Parasternal region		7 (12%)
Regional lymph nodes		7 (12%)
Distant metastases		13 (22·5%)
Pleura, lung, and mediastinum	5	
Bone	3	
Brain	1	
Liver	1	
Ovary	1	
Generalized	2	
Not stated		9 (15·5%)

Histological examination of both the original tumour and the recurrence was reported in 15 cases. In two cases the primary tumour alone was examined and in six cases the recurrence alone. In 35 cases no mention was made of histological examination. Of the nine cases given a histological label, five were described as scirrhous.

Now that the average expectation of life is increasing it seems reasonable to expect that similar cases of late recurrence will be met more frequently.

Summary

A case history is presented of a patient in whom widespread metastases from a carcinoma of the breast were first observed 35 years after radical mastectomy.

Similar cases in the literature are reviewed.

I wish to thank Dr. P. B. Woodyatt for permission to publish details of this case.

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Dr. UNA PORTER, senior psychiatrist at the Queen Victoria Hospital, Melbourne, and her brother, Mr. ALEC CATO, chairman of a manufacturing company and a chain of grocery stores, have offered the University of Melbourne £A.100,000 towards the cost of establishing a chair of psychiatry. Dr. Porter said she felt that a psychiatric chair was one of the university's urgent needs because medical studies were incomplete without it.

DESMOID TUMOUR OF CHEST WALL

BY

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AND

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Desmoid tumour (syn. desmoma; desmos–band) is a term applied to a general class of hard fibromas usually arising in the aponeuroses of the rectus abdominis muscle. Some 80 to 90% of cases occur in parous women, and this explains why injury is the generally accepted aetiological agent in the production of this type of lesion. In a few cases growths have appeared at the site of operation scars or after injury, but similar tumours were described in children of both sexes (Stout, 1954) and in cases where there does not appear to have been any pre-existing injury (Booher and Pack, 1951), and therefore there is still some doubt about their true aetiology.

Desmoid tumours occur as non-encapsulated nodular masses. In structure they vary from a hard acellular fibroma, relatively avascular, to the more cellular type which histologically resembles a well-differentiated fibrosarcoma. They exhibit infiltrative properties and produce atrophic changes in the tissues involved in the growth, but they are not malignant: metastases or sarcomatous changes have not been recorded, though recurrence after incomplete excision is not infrequent, especially in the more cellular type. Pagett called them "recurrent fibroids" (Boyd, 1947). Large desmoid tumours tend to degenerate, developing mucoid and cystic changes (Willis, 1948).

Extra-abdominal desmoids are rare: only a few reports have been published of their occurrence in the thoracic wall (Pearman and Mayo, 1942; Wiper and Miller, 1946; Musgrove and McDonald, 1948; Carty, 1954; Gatchell, Clagett, and McDonald, 1957; Nickell, Kittle, and Boley, 1958).

The cases reported here are, we believe, the first two thoracic desmoid tumours diagnosed and reported in this country.

Treatment is based on adequate surgical excision, although attempts have been made to treat them with antifibromatogenic hormones and *x*-ray therapy.

Case 1

A 54-year-old housewife was admitted to hospital in April, 1957, with a history of haemoptysis of two days' duration two years prior to admission, and another one a month prior to admission. She attended the chest clinic, where a radiograph revealed a round opacity in the lower zone of her right hemithorax. She had recently lost some weight and complained of cough. She has always been a heavy smoker. She had seven children, and all the deliveries, in her opinion, were difficult, the last one 14 years ago. She had a uterine prolapse operated on nine years before admission and has had extensive varicose veins on both legs for many years. Twelve months prior to admission she fell over a bicycle and heavily bruised the right side of her body, particularly her chest.

Physical examination revealed no abnormality except that there seemed to be diminished air entry over the right lower lobe and an area of dullness. There were no palpable glands anywhere.

Routine Laboratory Examinations.—Sputum: negative for tubercle bacilli. Urine: occasional leucocytes, no pus or casts; moderate growth of coliforms. Blood picture: R.B.C., 4,820,000/c.mm.; Hb, 14.35 g./100 ml.; Hb, 92% (Haden scale); colour index, 0.95; P.C.V., 41%; M.C.H.C., 35%; M.C.V., 85 cubic microns; W.B.C., 6,000/c.mm. (neutrophils 54%, eosinophils 3%, basophils 1%, monocytes 10%, lymphocytes 32%). E.S.R. 4 mm. in one hour (Westergren). Serum proteins: total 7% (albumin 4.1%, globulin 2.9%); A./G. ratio 1.41:1. Alkaline phosphatase, 14.5 units. Colloidal gold test was negative. Kunkel's test, 6 units.

Bronchoscopic examination revealed no abnormality, and the provisional diagnosis of a tumour in the right lower lobe was made. On April 11, 1957, a right thoracotomy was carried out. The chest was opened through the bed of the right fifth rib and a solid tumour 3 in. in diameter was found in the antero-lateral wall of the chest arising, as it appeared, from the intercostal muscle. The right lung was normal apart from a row of small nodules on the basal surface of the right lower lobe running towards the hilum. The tumour was resected together with the adjoining segments of the seventh and eighth ribs, including the intercostal structures. The chest was drained with a rubber intercostal tube and the wound closed in layers with braided nylon. The defect of the chest wall was repaired partly with a nylon darn. The drainage tube was removed on the third post-operative day, but because of an accumulation of fluid the chest was aspirated on the 10th (8 oz.; 227 ml.), the 15th (12 oz.; 340 ml.), and 22nd (20 oz.; 570 ml.) post-operative days. The patient was discharged on the 30th post-operative day with a "clear" *x*-ray picture and in good general condition.

She was seen at eight months and then two years later, when her general condition and radiograph were satisfactory and there was no evidence of a recurrence anywhere.

Pathology.—The gross surgical specimen consisted of a hard ovoid mass, unencapsulated, with a few muscle fibres attached to one edge and a small dark nodule at one end. The tumour was rubbery in consistence, the cut surface presenting interlacing bands of fibrous tissue giving a "whorled" appearance. Microscopically the bulk of the tumour was made up of dense wavy collagenous strands in which the cells were very sparse: there were no giant cells or mitotic figures present. The muscle fibres at the edge of the tumour were in the process of being engulfed by the fibres of the tumour, and showed varying degrees of degeneration. The small nodule consisted of collapsed haemorrhagic lung tissue infiltrated with inflammatory cells.

Case 2

A 49-year-old housewife, a nervous type, was admitted to hospital in September, 1958. About eight months prior to admission she noticed that she was very easily tired—"finished by midday." At that time she had a perineal rash said to be "due to nerves." Six months prior to admission she developed a feeling of tightness in the neck and a "burning" patch over the left side of her chest posteriorly.

A radiograph of her chest taken at the chest clinic revealed a round peripheral opacity in the right hemithorax, in close relation to the sixth and seventh ribs. On admission she complained of recurrent pain in that area and also an ache in the left parasternal area. She had had two normal deliveries and both children were then alive and well. Twenty years ago she had an appendix removed and recently a ganglion from her right wrist. On careful questioning she revealed that about six years before admission she had a bicycle accident, as a result of which she heavily bruised the left side of her face and left shoulder. Physical examination revealed a blood-pressure of 250/140, otherwise there was no abnormality in any system.

Laboratory Examinations.—Sputum: negative for tubercle bacilli and malignant cells. Culture resulted in a small growth of non-haemolytic streptococci and a heavy growth of *Proteus vulgaris*. Urine examination showed an occasional leucocyte, otherwise no abnormality. Blood picture: R.B.C. 5,100,000/c.mm; Hb, 14.51 g./100 ml.; Hb 93% (Haden scale); colour index, 0.91; P.C.V., 44%; M.C.H.C., 33%; M.C.V., 86 cubic microns; W.B.C., 4,400/c.mm. (neutrophils 53%, eosinophils 5%, basophils 0%, monocytes 8%, lymphocytes 34%). A few atypical plasma cells were present. E.S.R. 7 mm. in one hour (Westergren). Serum proteins: total 6.7% (albumin 4%, globulin 2.7%); A./G. ratio 1.48: 1. Alkaline phosphatase, 8 units. Colloidal gold test was negative. Kunkel's test, 6 units.

On October 7, 1958, an incision was made along the sixth rib. The pleura was found normal and therefore the chest was not opened. A lobulated tumour (2 by 1½ in.; 5 by 3.8 cm.) was found arising from the sixth intercostal bundle closely related to the adjoining ribs. The portions of the sixth and seventh ribs and the tumour were then resected and the wound was closed with nylon. The post-operative course was quite uneventful and the patient was therefore discharged home on the 11th post-operative day. Three months later she was readmitted with a discharging sinus in the thoracotomy wound which developed two weeks before readmission as a painful swelling along the wound. The sinus discharge revealed staphylococcal infection. The wound was then explored, and superficially infected tissues were excised. She was discharged home in good general condition with the wound completely healed nine days later.

Four months later she was readmitted again because of persistent pain over the area of the thoracic scar. A left thoracotomy was then performed, and it was found that the bone regenerating from the ends of the sixth and seventh ribs involved the intercostal nerve. The chest was opened. Parts of the sixth and seventh ribs, including the regenerating bone and intercostal nerve, were resected and the wound was closed with catgut and nylon. She was discharged home a month later in satisfactory general condition.

Pathology.—This tumour was ovoid in shape, measuring 2 by 1½ by ½ in. (5 by 3.8 by 1.3 cm.), with muscle attached to the deeper side and resting in a smooth eroded cavity in the rib. The tumour had no true capsule, the smooth surface in contact with the rib consisting of fibrous tissue merging into the rest of the tissue. It bulged when cut, the surface presenting a glistening appearance with faint brownish-yellow septa, dividing the tumour into smooth lobules. The microscopical appearance was that of interlacing strands of dense fibrous tissue: moderately cellular, the cellularity varying in different parts of the tumour. Some of the individual cells were plump, but the majority were typical spindle cells. No giant cells or mitotic figures were seen. The skeletal muscle attached to the tumour was diffusely infiltrated by strands of fibrous tissue. The muscle bundles and fibres showed various stages of degeneration as evidenced by swelling, loss of striation, and decrease in the number of nuclei. A few normal nerve bundles were present in the loose tissue surrounding the tumour. The rib showed no gross histological changes.

Examination of the tissues removed at the second operation disclosed the following conditions: (*a*) A nodule at the peripheral end. This showed regenerating bone and cartilage with a tumour mass similar in histological appearance to the original tumour, infiltrating bone, cartilage, and muscle, the latter showing the same degenerative changes as previously described. A few small giant cells were present, especially in those parts adjacent to the cartilage. Some nerve bundles were entangled in the heterogeneous mass. The tumour was moderately cellular and vascular. (*b*) Spinal end: dense fibrous tissue with a few degenerating muscle fibres. (*c*) Tissue adjacent to the periosteum: dense acellular interlacing collagenous fibres.

Discussion

In the above two cases the tumours conformed to the accepted pattern of a desmoid tumour. They consisted mainly of interlacing bundles of fibrous tissue infiltrating into the adjacent structures and producing atrophic

changes in these tissues. Case 1 represents the acellular type, and Case 2 the more cellular type which recurred probably as the result of incomplete resection in the first instance. Neither case showed histological evidence of sarcomatous change, and so far there has been no evidence of metastases. There was a history of previous injury in both cases, but the women were past the climacteric. It may be that hormone disturbances bore some relation to development of the tumours.

Summary

Two multiparous women were operated on for a solid tumour in the chest wall. There was a history of injury in both cases, and histological examination of the resected specimens revealed a desmoid tumour arising from the intercostal tissue. The tumour was resected with the adjoining portion of the chest wall, and no recurrence had occurred in 24 and 12 months later respectively.

This paper is published because we believe that these are the first two cases of desmoid tumour of the chest diagnosed and reported in this country.

We thank Mr. B. B. Milstein and Mr. R. Rowlandson, the thoracic surgeons, for permission to report their cases.

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Medical Memoranda

A Case of Amoebic Brain Abscess

Since Morehead's (1838) original observation of a brain abscess associated with tropical liver abscess and the demonstration by Kartulis (1904) of amoebae in the brain, amoebic brain abscess has been recognized as a rare complication of amoebiasis. Orbison *et al.* (1951) were able to collect 83 reports of the condition, of which the diagnosis was authenticated by the demonstration of amoebae in the lesions in 22. To these they added five cases, in three of which amoebae were found. Since then at least four further cases have been reported (Koshy, 1950; de la Maza and Guzman, 1953; Kirk, 1956; Lenshoek *et al.*, 1958), in three of which amoebae were found in the cerebral lesions. Of this total of 92 cases, only 10 were presumed to have been unassociated with lesions in the liver or lung, and only five of these were proved by the finding of *Entamoeba histolytica* in the brain abscess.

Case Report

An African man aged 35, previously in good health, complained that on waking, four hours before admission, he felt numbness of the right side of the body. On getting out of bed he was unable to walk because of right-sided weakness. He also noticed involuntary movements of the right hand.

On examination his temperature was 99° F. (37.2° C.). He was mentally normal. There was weakness of the right arm and leg, and the right knee-jerk was brisker than the left. Involuntary supination and pronation of the right hand was present. There were no other abnormal physical signs. The C.S.F. findings were: pressure, normal; cells, absent; globulin, increased; protein, 200 mg./100 ml.; chlorides, 720 mg./100 ml., sugar, 92 mg./100 ml.; culture, sterile. Blood and C.S.F. Wassermann reactions were negative. A provisional diagnosis of cerebral thrombosis was made. There was little change in the patient's condition until the third day, when his temperature rose to 102° F. (38.9° C.), and he began to pass dysenteric stools in which trophozoites of *E. histolytica* were found. With the possibility of brain abscess in mind, treatment was begun with emetine, chloroquine sulphate, diiodohydroxyquinoline, and tetracycline. A further lumbar puncture showed: xanthochromic fluid under normal pressure; 48 lymphocytes and 80 polymorphonuclears per c.mm.; globulin, markedly increased, protein, 400 mg./100 ml.; chlorides, 700 mg./100 ml.; sugar, 86 mg./100 ml.; culture, sterile.

The patient's dysenteric symptoms improved, but the hemiparesis became more severe. On the sixth day he became stuporous. Cerebral angiography was then done. This showed distortion and displacement of the left internal carotid artery. The vessels were stretched and filled poorly. The displacement indicated a space-occupying lesion in the temporoparietal region. Death occurred eight hours after angiography.

Necropsy was done approximately 20 hours after death. Significant pathological findings were noted in the brain, caecum, and rectum.

Brain.—A localized yellow exudate was found in the leptomeninges of the left parietal lobe. On removing the brain, rupture of part of this region occurred, and thick yellowish-green material escaped. Coronal section through the cerebrum showed a large left parieto-temporal abscess containing thick yellowish-brown exudate. Strands of necrotic brain tissue were present in the cavity, which extended from about the midline to the lateral wall of the cortex, perforating it in one area. The left lateral ventricle was compressed and displaced medially. The abscess wall was ragged and yellowish-grey in colour (Fig. 1), while the surrounding brain showed areas of haemorrhage but no signs of a limiting membrane. These features suggested an amoebic brain abscess. A wet preparation of the abscess contents, examined at the Amoebiasis Research Unit, disclosed numerous motile *E. histolytica*. Microscopical examination of sections showed a central area of necrosis, surrounded by neutrophils, lymphocytes, and mononuclear cells, in which amoebae were present (Figs. 2 and 3). The surrounding brain tissue showed haemorrhage and necrosis but no evidence of repair.

Fig. 1.—Portion of cerebrum showing ragged surface of abscess wall.

Large Intestine.—The caecum showed two ulcers about 1 cm. in diameter with undermined edges. Two small nodules having minute openings and containing yellow exudate were present in the rectum. Though the condition was macroscopically typical of amoebic ulcers, microscopical

examination of sections of the caecum showed necrosis of the mucosa and part of the submucosa with undermining at the edges, but no amoebae were seen.

No abnormality was found in sections of lung, liver, and kidney.

Comment

In Durban, where acute and severe amoebiasis is extremely common among Africans, the rarer complications of the disease occur often enough for them to be of clinical importance. We have records of two further cases of brain abscess which were presumed to be of amoebic aetiology. One occurred in a male infant aged 5 months, and the other in a 47-year-old man. Despite antiamoebic therapy, both died. In both instances there was an associated liver abscess, as in the great majority of cases reported previously (Roach, 1958). The condition might be demonstrated more often if the contents of brain abscesses were examined by wet preparation in all cases in an endemic area.

The present case is of interest because initially the condition simulated hemiparesis due to cerebral thrombosis, and as there was no evidence of hepatic or pulmonary involvement the diagnosis of amoebic brain abscess was considered only when the patient developed symptoms of amoebic dysentery. Most recent reports of isolated amoebic brain abscess suggest that *E. histolytica* may reach the brain by way of the paravertebral plexus of veins (Stein and Kazan, 1942; Halpert and Ashley, 1944; Koshy, 1950), though it is impossible, despite most careful examination, to be certain that microscopic lesions in the liver are not present, or were not present before amoebicidal drugs were given.

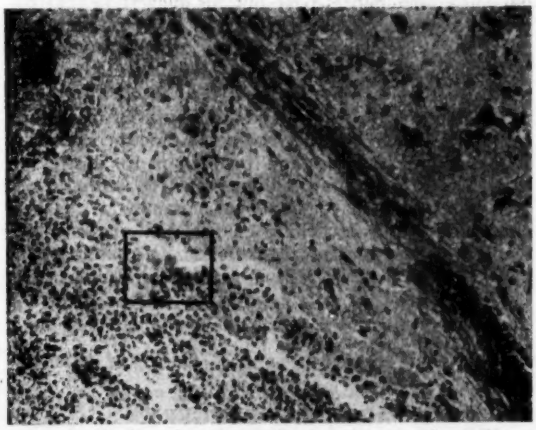

Fig. 2.—Section of cerebrum showing abscess and amoeba.

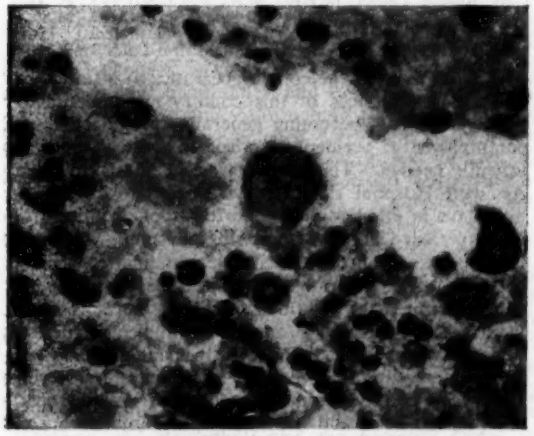

Fig. 3.—Amoeba (portion enclosed in Fig. 2). (×745.)

The prognosis of amoebic brain abscess is extremely grave. Only three reported cases have survived (Robles, 1943; Collard and Kendall, 1947; Lenshoek *et al.*, 1958). In two of these cases *E. histolytica* was not found in the cerebral lesions, and response to emetine was regarded as an important diagnostic feature. In the case reported by Robles the patient underwent surgery, and no details of medical treatment are given. It is perhaps noteworthy that numerous motile amoebae were found in the abscess contents of our case despite four days of antiamoebic therapy. Whereas emetine and chloroquine are known to be concentrated in the liver and are therefore effective in amoebic liver abscess, there is no evidence that they reach amoebicidal concentrations in the brain, where it has been shown that the concentration of both is low (Berliner *et al.*, 1948; Parmer and Cottrill, 1949). At present it is doubtful whether we possess any drug that has much effect on this condition.

We thank Dr. S. Disler, medical superintendent, King Edward VIII Hospital, for permission to publish this case, and Dr. G. Roach, acting deputy head of the department of pathology, for allowing us to quote the other two cases.

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Hungary, which has a population of ten million, is to build 19 new hospitals in the next five years according to the draft plan for 1961 to 1965 submitted by the Ministry of Health to the National Planning Office. In addition the Ministry hopes to build seven tuberculosis institutes, 32 specialist surgeries, seven public health and epidemic stations, 15 homes for old people, and extensions to three medical universities. Though the country already has one doctor for every 650 people—one of the highest rates in the world—the proportion is to be bettered in the five years to one for 550.

Reviews

CULTURE AND MENTAL HEALTH

Culture and Mental Health. Cross-cultural Studies. Edited by Marvin K. Opler. (Pp. 533+xxi. 61s.) New York and London: The Macmillan Company. 1959.

"Culture" is one of the key-concepts of social anthropology which has passed into the general vocabulary of educated people in the United States and countries deriving their social sciences therefrom, though it has a much more restricted use in Great Britain. Its definition is a matter of semantic squabbles; but it includes all the behaviour, responses, and values which are learned through membership of a given society and —by most definitions—excludes the genetic inheritance of the members of the society and the raw materials which have not been modified by human activity. It is this meaning of the word which has been employed by the editor and his 22 contributors of the book under review, which is published in connexion with the current World Mental Health Year. Nineteen of the contributors are American, two (Dr. Carstairs and Dr. Loudon) British, one Formosan, and one (Dr. H. B. M. Murphy) whose nationality is not clear, though his training was British. His essay, "Culture and Mental Disorder in Singapore," is one of the most distinguished in the volume.

Theoretically, culture can impinge on the concept of mental health and mental disorder in a number of ways, all of which are illustrated to a certain extent in this volume. The norm, by which mental health is judged, is in very many ways a cultural artifact; the well-adjusted in one culture will be the deviant in another. The identification of, tolerance for, and techniques of therapy of mental disorder are all culturally determined; and some of the most entertaining papers describe non-European techniques of therapy, the dream analyses of the Iroquois and Ute (Amerindians), the group therapy of the Zar of Abyssinia, and the links between psychological stresses and religious ritual among the Zulus or the Hindus of North India. Finally, and this is the most relevant aspect for medical practitioners, there seems to be a close connexion between the stresses developed within certain cultures and the form and incidence of mental disorders. In a summary, Dr. Wittkower and Dr. Fried, of McGill University, write:

> "Suggestive evidence has been submitted to substantiate the hypothesis that cultures differ significantly in incidence and symptomatology of mental illness. The available evidence strongly suggests that cultures differ (*a*) in the amount of aggression, guilt, and anxiety generated within the structure of the life situations faced, and (*b*) in the techniques used by the members of these cultures in dealing with aggression, guilt, and anxiety. These areas require further elaboration. Such sociocultural variables as family and community organization, rapid sociocultural changes, migration, population pressure, and political events are undoubtedly related to the etiology of mental illness."

The most important papers in this collection are those which analyse the incidence or severity of various types of mental illness among groups of people of different cultural origins who have been hospitalized in the same area during a short period of years, and attempt to link the incidence of mental illness with the known facts about the different cultural backgrounds. Outstanding among these are Dr. Murphy on the Indians, Chinese, and Malays of Singapore; the editor, Dr. Opler, on the differing forms of schizophrenias observed in New York in 1954 among patients born in Southern Italy and in West Ireland; Dr. Sanua on the differences of personality adjustment of American Jews and Gentiles, according to the number of generations the family has been in the United States; Dr. Jaco on the Mexicans, "Anglos," and Negroes in Texas; and a very impressive study by Dr. Fried on the stresses resulting in Indians from the migration from the highlands of Peru to the plains. These papers are all informative; and they suggest that diagnosis and prognosis of mental illness might be considerably advanced if the cultural background of patients were to be made a regular part of all case-history material.

A collection of essays, such as this, which aims at great geographical and disciplinary inclusiveness, is something of a rag-bag. Besides the essays referred to, attention can be called to Dr. Caudill's "Observations on the Cultural Context of Japanese Psychiatry"; Dr. Carstairs' "The Social Limits of Eccentricity: An English Study," with its short historical résumé of the great changes in the history of the care of the mentally ill in England, and its suggestive study on the reintegration into social life of formerly committed patients (other papers bear out his suggestion that the recovered psychotic needs the support of numerous, but not too closely related, adults); and Dr. Margaret Mead's summary, "Mental Health in World Perspective."

The bias of the editor and his contributors is to a somewhat eclectic approach to psychiatric theory, to the school of Adolf Meyer; and it is perhaps for this reason that there are no contributions from the distinguished Americans who have used psycho-analytic concepts consistently in approaching cultural material, such as Dr. Erik Erikson or the late Professor Kluckhohn. Probably few except reviewers will read this collection from cover to cover; but all who are interested in the diagnosis or treatment of mental illness can find some papers to interest them.

Geoffrey Gorer.

ACCIDENT SURGERY

Modern Trends in Accident Surgery and Medicine. Edited by Ruscoe Clarke, M.B.E., M.B., F.R.C.S.(Eng.), F. G. Badger, B.Sc., F.R.C.S.(Ed.), and Simon Sevitt, M.D., M.Sc., F.R.C.P.I., D.P.H. (Pp. 330+xi; illustrated. 75s.) London: Butterworth and Co. (Publishers) Ltd. 1959.

This book makes a welcome appearance at a time when the accident services of this country are under active review, and it is becoming generally recognized that a comprehensive accident service for the country is urgently needed. The pioneer work of the Birmingham Accident Hospital since 1941 is well known, and we now have in this book an opportunity of profiting from the experience of the staff of that hospital. Although it does not set out to be a complete manual on accident surgery, yet a wide range of subjects has been covered. Limb fractures are described fully, and there are sound, workmanlike chapters on other subjects such as abdominal and chest injuries, facio-maxillary, and peripheral nerve injuries. Burns and anaesthesia which have been considered in other books from this centre are omitted here, and head and spinal injuries are not included. A high and even standard has been maintained throughout. Two chapters written by Mr.

Ruscoe Clark, to whom this volume is unhappily a memorial, should be mentioned particularly. His reinterpretation of the principles of wound surgery and his criticism of the formal wound excision which so many surgeons learned in two previous wars will provoke discussion but is backed by a wide experience; and his plea for massive blood transfusion in severe injury will certainly awaken many readers to the need for careful appraisal of blood loss and to the severe losses that can take place.

There is, however, more in this volume than a careful and reliable guide to the treatment of many common injuries. It shows clearly in such chapters as those on the circulatory responses to injury, traumatic uraemia, and thrombosis the scope which exists for research in trauma and how much awaits to be done. There is more in the treatment of trauma than surgery. It demands the combined efforts of physicians, pathologists, biochemists, and others to unravel the problems of the body's reaction to injury, and the mechanisms of repair. Doctors attracted to this field will know that they are now dealing with one of the commonest causes of morbidity and mortality in the country to-day.

This book will be read and used by all those responsible for the organization of accident services, and by surgeons treating accident cases. In congratulating the authors and the publishers on this stimulating and well-produced book, its major contribution may well prove to be its demonstration of the breadth of modern accident surgery and medicine.

WALPOLE LEWIN.

BIOCHEMISTRY OF INJURY

The Biochemical Response to Injury. A Symposium Organized by C.I.O.M.S. Edited by H. B. Stoner, with the assistance of C. J. Threlfall. (Pp. 467+xi; illustrated. 57s. 6d.) Oxford: Blackwell Scientific Publications. 1960.

This volume is based on papers given at an important conference on the biochemistry of injury organized in 1958 by the Council for International Organizations of Medical Sciences (C.I.O.M.S.)—itself an offshoot of U.N.E.S.C.O. and W.H.O. Experts from many countries took part, and this book thus provides a unique summary of recent knowledge and opinion on the subject. Since each contributor approached the topic from a different aspect of interest and with different experimental techniques the edited discussions following each paper are particularly valuable in providing a sense of proportion to the individual viewpoints. Biochemical changes inside cells, across cell membranes, across capillary membranes, and in blood cells as well as the systemic changes throughout the body were all considered. Injuries included cold, heat, ultra-violet radiation, chemicals, bacterial toxins, and ischaemia, and though there are differences in the findings after such varied assaults there are clearly sufficient similarities to warrant the concept of a common response or series of responses to injury.

Of general interest are the sections on the mediation of changes of capillary permeability (Miles and Wilhelm); the effects of bacterial injury (Smith) and changes of carbohydrate (Stoner and Threlfall), protein (Cuthbertson), and water metabolism (Wynn). More controversial, at least in their application to therapy, are the sections on electrolyte disturbances in burns (Millican and Rosenthal) and the bacterial factor in traumatic shock (Fine and others). The editors are to be congratulated on having brought together in readable and sufficiently uniform style so many different approaches to research on response to injury. This book can be recommended as probably the best general account of the topic at present available; and it is likely to remain so for a considerable time.

J. P. BULL.

CERVICAL CANCER

Cancer of the Cervix: Diagnosis of Early Forms. In Honour of Dr. C. Kaufman. Ciba Foundation Study Group No. 3. Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and Maeve O'Connor, B.A. (Pp. 114+viii; illustrated. 12s. 6d.) London: J. and A. Churchill, Ltd. 1959.

The third Ciba Foundation Study Group, on the diagnosis of early forms of cancer of the cervix, was held on May 8, 1959, in honour of, and around the work of, Professor Kaufmann, of Cologne, with Professor W. C. W. Nixon in the chair. Authorities in this field from Europe and the United States joined with their British colleagues in discussing the many aspects of this problem. There were six formal papers, each of which provoked keen discussion. Much of the time was spent in attempting to define the difference between carcinoma *in situ* and early invasive carcinoma, but even chromosomal and cytoplasmic cytopathology as revealed by both optical and electron microscopy offered no definitive criteria. Mr. Lawson described the activity of the enzymes β-glucuronidase and α-mannosidase in the vaginal fluid. Both enzymes were usually more active in association with cancer, but this line of approach, although simpler and more objective, is at present associated with a 20% error each way in premenopausal women.

There was general agreement concerning the means of detecting carcinoma *in situ*, which included Schiller's iodine test, cytological screening, the colpascope, and some form of biopsy. Fifty per cent. of all cases of carcinoma *in situ* are detected in women between the ages of 16 and 35, of whom less than half have invasive carcinoma. All were agreed that simple procedures such as multiple biopsy or conization sufficed in the younger group of patients, provided that they were cytologically screened at frequent intervals. The crux of the problem is the adequate follow-up in the average gynaecological centre.

The only error noted is on p. 85, where in the eighth line of the fourth paragraph the age 23 should be 35 (see p. 88). Dr. Wolstenholme, assisted by Miss O'Connor, has ably edited a book worthy of its predecessors, which should be read by all gynaecologists. Medicine's debt to the Ciba Foundation increases annually.

G. W. THEOBALD.

ENCEPHALITIS AND VACCINATION

Postvaccinial Perivenous Encephalitis. A Pathological Anatomical Study on the Place of Postvaccinial Perivenous Encephalitis in the Group Encephalitides (The Disease of Turnbull—Luksch—Bastiaanse). By Ernst de Vries. (Pp. 181. +vii; illustrated. 38s.) Amsterdam, London, New York, Princeton: Elsevier Publishing Co. 1960.

The wave of post-vaccinial neurological complications which began in 1922 and reached its maximum in 1930 has provided researchers with a unique opportunity to study the pathology of encephalitis, unique because the one agent which is constantly concerned in, or at any rate associated with, its production is a known

attenuated virus. Nervous sequelae of smallpox vaccination had been known certainly since the year 1802 but the first established instance of perivenous encephalitis, now generally regarded as characteristic of the disease, dates from 1912, the case having been reported by Turnbull and McIntosh in 1926, since when a considerable literature has accumulated.

No one has devoted more time and thought to this condition than Dr. de Vries, so this monograph, based as it is on his study of 62 cases and a thorough search of the literature, is most welcome and useful. He regards "perivenous microglia encephalitis" as a clinico-pathological entity and as the characteristic histological reaction type following smallpox vaccination, although it may follow other exanthemata or even other diseases; it differs, he says, from encephalitis caused by a living agent and from the usual reaction to toxic and infectious conditions, and it does not occur under the age of 2. However, not all neurological fatalities following smallpox vaccination take this histological form, and the range of findings he describes make interesting reading and provide important food for thought.

W. H. McMenemey.

AMERICAN PRIMER

Clinical Epidemiology. By John R. Paul, M.D., Sc.D. (Pp. 291+xii; illustrated. 37s. 6d.) Chicago: University of Chicago Press. London: Cambridge University Press. 1958.

Epidemiology is a science concerned with the circumstances under which sickness occurs in a community, but for many years the term has been used in a more restricted sense as applicable only to the study of communicable diseases. Following the lead of John Ryle, who used the term "social pathology" to describe studies of the relationship of disease prevalence to social, environmental, and genetic factors, a significant minority of practising doctors now use epidemiological methods in studying the aetiologies of a wide range of non-infective diseases—e.g., cancers, hypertension, coronary thrombosis, peptic ulcer, mental disorders. British workers have been pioneers in this kind of clinical epidemiology or, to give it another name, social medicine, which, like psychiatry, is now becoming a respectable and respected medical specialty.

Professor John Paul has been one of the American apostles of the new gospel, and in this small book his purpose—in which he succeeds reasonably well—is to introduce this "new look" in epidemiology to a wider audience of doctors and students of medicine, biology, or sociology. After a brief historical review, he deals (for the most part in non-technical jargon) with the aetiological triad—the seed, the soil, and the environment (or climate), methodology including the new developments in serological surveys, and the contributions of experimental epidemiology. As examples, he has chosen four infective conditions, rheumatic fever, poliomyelitis, hepatitis, and the arthropod-borne virus infections, and one non-infective condition, coronary occlusion, and that not very up to date. This is the weakness of the book for a British audience which might have preferred more of the non-infectious examples. However, as the author remarks, it is easier to learn from the classical studies on infectious diseases, and we may hope that this American primer will interest a wider public in the methods and merits of group research in medicine.

Robert Cruickshank.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Typical Gynecologic Operations. With Special Considerations of Technical Advantages. By Dr. Siegfried Tapfer. Translated by L. M. Szamek, M.D. (Pp. 81; illustrated. 72s.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co., Ltd. 1960.

The Kybernetics of Natural Systems. A Study in Patterns of Control. By D. and K. Stanley-Jones. (Pp. 145+xii. 42s.) London, Oxford, New York, Paris: Pergamon Press. 1960.

Nonpenetrating Injuries of the Abdomen. By Robert H. Kennedy, B.A., M.D., F.A.C.S. (Pp. 121+vii. 38s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Hypothermia in Surgical Practice. By K. E. Cooper, M.Sc., M.B., B.S., and D. N. Ross, B.Sc., M.B., Ch.B., F.R.C.S. (Pp 116+xi; illustrated. 18s. 6d.) London: Cassell. 1960.

Die Kunstliche Insemination. By Dieter Giesen. (Pp. 49. DM. 3.80.) Trier: Paulinus-Verlag. 1960.

Neurochemistry of Epilepsy: Seizure Mechanisms and their Management. By Donald B. Tower, M.D., Ph.D. (Pp. 335+x; illustrated. 72s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Mechanisms in Radiobiology. Edited by Maurice Errera and Arne Forssberg. Volume II: ***Multicellular Organisms.*** (Pp. 395+xiv; illustrated. $13.) New York and London: Academic Press. 1960.

Demonstrations of Physical Signs in Clinical Surgery. By Hamilton Bailey, F.R.C.S.(Eng.), F.A.C.S., F.R.S.Ed. Thirteenth edition. (Pp. 928+xiv; illustrated. 75s.) Bristol: John Wright and Sons, Ltd. 1960.

Psyche und Hormon. Einführung in die Endokrine Psychosomatik, Psychoanalytische Klinik und Lehre vom Stress. By Heinrich Meng, with Charles A. Joël, Heinrich Meng, Paul Parin, Hans Selye, and Felix G. Sulman. (Pp. 486+xix; illustrated. DM. 78.) Berne and Stuttgart: Hans Hueber. 1960.

Prematurity. The Diagnosis, Care and Disorders of the Premature Infant. By Beryl Corner, M.D.(Lond.), F.R.C.P. (Lond.). (Pp. 587+xiii; illustrated. £5 5s.) London: Cassell. 1960.

Asexual Propagation and Regeneration. By M. A. Vorontsova and L. D. Liosner. Translated from the Russian by P. M. Allen. Edited by F. Billett. (Pp. 489+xxiv; illustrated. 70s.) London, Oxford, New York, Paris: Pergamon Press. 1960

Marriage: East and West. By David and Vera Mace. (Pp. 352. 30s.) London: Macgibbon and Kee. 1960.

Diseases of the Nervous System: In Infancy, Childhood and Adolescence. By Frank R. Ford, M.D. Fourth edition. (Pp. 1,548+xvi; illustrated. £11 16s.) Oxford: Blackwell Scientific Publications. 1960.

Chemical Micromethods in Clinical Medicine. By R. H. Wilkinson, M.A., M.D. (Pp. 121+xiv; illustrated. 40s.) Oxford: Blackwell Scientific Publications. 1960.

Controlled Clinical Trials. Papers Delivered at the Conference Convened by C.I.O.M.S. Organized under the direction of Professor A. Bradford Hill, F.R.S. (Pp. 177+vii; illustrated. 20s.) Oxford: Blackwell Scientific Publications. 1960.

Carcinoma of the Thyroid Gland. A Clinical and Pathologic Study of 293 Patients at the University of California Hospital. By Stuart Lindsay, M.D. (Pp. 168+x; illustrated. 68s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

A Dictionary for Medical Secretaries. By Isabel Alice Stanton. (Pp. 175+viii. 52s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

English for the Foreign Physician. By José Murilo Martins, M.D. (Pp. 121+xi; illustrated. 46s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The Chemical Senses in Health and Disease. By H. Kalmus, Sc.D., M.D., and S. J. Hubbard, B.Sc., Ph.D. (Pp. 95+vii; illustrated. 30s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

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AUTO-ANTIBODIES AND LUPUS ERYTHEMATOSUS

The Greek sea-god Proteus had the habit of appearing in numerous different disguises to the confusion of his enemies. W. Bauer and his colleagues[1] have drawn attention to the protean nature of the so-called connective tissue diseases, the most versatile of which is undoubtedly disseminated lupus erythematosus. The kaleidoscope of involvement of many organs and systems is often the most characteristic feature of the characteristic case—a point made by speakers at the symposium held last week during the Annual Clinical Meeting of the B.M.A. at Middlesbrough (see p. 1147). But what is the characteristic case? The clinical concept, to quote E. G. L. Bywaters,[2] is of "a generalized and usually fatal disease described first by Kaposi in 1872. It affects connective tissues throughout the body and is characterized by an erythematous macular rash, by serositis, nephritis, arthritis, enlargement of lymph nodes, splenomegaly, purpura, and leucopaenia." To this list might be added pulmonary infiltrations, Libman-Sacks endocarditis, Raynaud's disease, Mikulicz's syndrome, epilepsy, polyneuritis, and a host of other clinical presentations, alone or in mixed groups.

With such variability the unity of the condition is in doubt, and a single determining cause seems hardly possible. Nevertheless, other diseases—for example, tuberculosis and syphilis—express themselves in a protean manner and do not offend against the doctrine of specific causality. Pott's disease and scrofula, and tabes and crural gummata, might seem independent if we did not know the microbial common denominators. For lupus erythematosus there is as yet no such common denominator. P. Klemperer's[3] use of the term "collagen diseases" drew wider attention to the similarities between disseminated lupus and rheumatoid arthritis, dermatomyositis, and polyarteritis, in all of which widespread fibrinoid necrosis of collagen may occur. The term is now obsolete, since necrosis of collagen may be seen in any destructive process, such as abscess or peptic ulcer. Parenthetically, the only true collagen disease is probably the rare condition described by S. L. Baker and H. M. Turnbull[4] resembling osteomalacia, in which collagen fibrils of abnormal appearance are produced. If, therefore, the concept of a diffuse collagen disease is no longer tenable, the theory that disseminated lupus (and related disorders) results from generalized auto-immune reactions becomes more attractive. What then is the evidence that auto-antibodies occur in or cause this disease?

Histologically, the most specific sign of disseminated lupus is perhaps the appearance of haematoxylin bodies, now believed to represent fragments of cell nuclei lying free in the tissues. Unfortunately these may be absent from, or difficult to find in, the mild, acute, or early case. Other lesions, such as the "wire loop" appearance of renal glomerular capillaries, are specific only for a particular organ, which may or may not be involved. When the Hargraves[5] test for "lupus cells" was described in 1948, many hoped that it might prove to be the hallmark of the disease. Indeed, many acted and wrote as though a positive test automatically implied disseminated lupus, its absence excluding it. This has not proved to be so, and nearly all who have studied post-mortem series have noted a proportion of cases with histological findings of typical fibrinoid necrosis and haematoxylin bodies in whom, in life, the lupus cell phenomenon could not be detected. Conversely, a small proportion of patients with otherwise indistinguishable rheumatoid arthritis will show a positive lupus-cell test.[6]

Although the study of the lupus cell phenomenon has proved disappointing in achieving a more precise definition of the disease, it has been a stimulant to the elucidation of the disordered immunological

[1] Bauer, W., Giansiracusa, J. E., and Kulka, J. P., in *Rheumatic Diseases*, Ed. C. A. Slocumb, 1952, Philadelphia, p. 391.
[2] Bywaters, E. G. L., in *Paediatrics for the Practitioner*, Ed. W. Gaisford and R. Lightwood, 1954, London, vol. 3, p. 610.
[3] Klemperer, P., Pollack, A. D., and Baehr, G., *J. Amer. med. Ass.*, 1942, **119**, 331.
[4] Baker, S. L., and Turnbull, H. M., *J. Path. Bact.*, 1950, **62**, 132.
[5] Hargraves, M., Richmond, H., and Morton, R., *Proc. Mayo Clin.*, 1948, **23**, 25.
[6] Hijmans, W., Kievits, J. H., and Schuit, H. R. E., *Acta med. scand.*, 1958, **161**, 341.
[7] Holman, H. R., Deicher, H. R. G., and Robbins, W. C., in *The Mechanism of Hypersensitivity*, Ed. J. H. Shaffer, G. A. Lo Grippo, and M. W. Chase, 1959, London, p. 361.
[8] Haserick, J. R., Lewis, L. A., and Bortz, D. W., *Amer. J. med. Sci.*, 1950, **219**, 660.
[9] Robineux, R., in *The Mechanism of Hypersensitivity*, Ed. J. H. Shaffer, G. A. Lo Grippo, and M. W. Chase, 1959. London, p. 371.
[10] Holborow, E. J., Weir, D. M., and Johnson, G. D., *Brit. med. J.*, 1957, **2**, 732.
[11] —— *Proc. roy. Soc. Med.*, 1960 (in press).
[12] Thomas, Lewis, *J. chron. Dis.*, 1959, **10**, 428.
[13] Kellgren, J. H., and Ball, J., *Brit. med. J.*, 1959, **1**, 523.
[14] Moore, J. E., Shulman, L. E., and Scott, J. T., *J. chron. Dis.*, 1957, **5**, 282.
[15] Gadjusek, D. C., *Nature (Lond.)*, 1957, **179**, 666.
[16] Asherson, G. L., *Brit. J. exp. Path.*, 1959, **40**, 209.
[17] Deicher, H. R. G., Holman, H. R., and Kunkel, H. G., *Arthr. Rheum.*, 1960, **3**, 1.
[18] Mackay, I. R., Taft, L. I., and Cowling, D. C., *Lancet*, 1959, **1**, 65.
[19] Dubois, E. L., *Ann. intern. Med.*, 1956, **45**, 163.
[20] Rupe, C. E., and Nickel, S. N., *J. Amer. med. Ass.*, 1959, **171**, 1055.
[21] Jalil, M. J., Armas Cruz, R., Harnecker, J. J., and Gonzalez, F., *Rev. méd. Chile*, 1958, **86**, 717.

process. H. R. Holman, H. R. G. Deicher, and W. C. Robbins[7] have drawn attention to the clinical evidence for circulating auto-antibodies, including "haemolytic anaemia with positive Coombs test, a leukopaenia with accompanying leuko-agglutinins, a thrombocytopaenic purpura, a false positive serologic test for syphilis, a circulating gamma globulin, which interferes with clotting, and kidney lesions, in which there is a deposition of gamma globulin in the glomerulus," in addition to the lupus-cell phenomenon. J. R. Haserick, L. A. Lewis, and D. W. Bortz[8] showed that a specific gamma globulin now called the lupus factor was responsible for lupus-cell formation, and could cause the *in vitro* swelling and extrusion of the cell nucleus, which was then taken up by a phagocyte as an inclusion body. R. Robineux[9] has beautifully demonstrated the whole sequence of changes *in vitro* by time-lapse cinematography.

That the lupus factor is an antibody in the conventional sense is mainly a matter of definition. It answers all the criteria for an antibody except that of specificity. Avian, mammalian, or reptilian nuclei are all attacked by this factor. Originally it was thought that the lupus factor might be identified as an antibody to nucleoprotein, but when this was tested—for example, by the technique of E. J. Holborow, D. M. Weir, and G. D. Johnson,[10] who used a fluorescent anti-globulin method for demonstrating lupus-factor nuclear conjugates—it was found that this explanation was too simple. Other anti-nuclear factors were discovered in sera which did not contain the lupus-cell factor. These include antibodies to desoxyribonucleic acids and to histone and possibly to other nuclear constituents occurring singly or together.[7] Other associations of antibodies have been seen—thus E. J. Holborow and his co-workers[11] recently reported to the Royal Society of Medicine that anti-nuclear factors had been found in the sera of some patients with Hashimoto's thyroiditis. Conversely, some patients with lupus may possess thyroid antibodies.[12] A similar overlap is seen between lupus and rheumatoid arthritis: While 10% or so of rheumatoid sera will show anti-nuclear factors,[11] about 30 to 50% of lupus sera show a positive Rose–Waaler test based on an anti-gamma-globulin reaction, and characteristic of rheumatoid arthritis.[13]

Another curious immunological phenomenon was explored by J. E. Moore, L. E. Shulman, and J. T. Scott.[14] A number of patients with persistent false-positive serological tests for syphilis were found to develop signs of lupus later. As a group their lupus was very mild, yet it could occasionally progress to severe disease after many years. Tests for syphilis depend on the presence of a substance acting like a non-specific antibody to certain tissue extracts, and a parallel with the anti-nuclear auto-antibodies becomes more obvious.

Yet another method of investigating auto-antibodies has been cleared up by D. C. Gadjusek,[15] using complement fixation methods. G. L. Asherson[16] has demonstrated by these means antibodies to isolated mitochondria and soluble cellular proteins in disseminated lupus, as well as (here the overlap shows again) in macroglobulinaemia and syphilis. H. R. G. Deicher, H. R. Holman, and H. G. Kunkel[17] have extended this work and have also shown antibodies to microsomes. In elegant experiments they have demonstrated conclusively that the reaction observed between microsomes and lupus sera is not due to contamination with nuclear material, and is chemically distinct from anti-microsomal reactions observed in other diseases. However, the lack of correlation between the amount of such "auto-antibodies," whether anti-nuclear or anti-cytoplasmic, and the extent of disease has led most of these authors to believe that the reactions they are observing indicate an unusual state of the immune-antibody-producing system rather than a cause of the disease. Thus it is becoming clear that the lupus-cell phenomenon is but one of many queer auto-immune reactions found in disseminated lupus, but not necessarily specific for it. While this conclusion is not helpful in the search for a definition of disseminated lupus, it gives a new perspective on such conditions as "lupoid hepatitis,"[18] in which a positive lupus-cell test has been found in association with the so-called juvenile cirrhosis of the liver.

It is against this background of clinical and serological variability of lupus, and of increasingly used tests and increasing numbers of tests, that reports on the treatment and progress of the disease must be judged. From such reports one might infer that disseminated lupus is becoming more common,[19] more benign,[20] and more responsive to treatment.[21] In C. E. Rupe and S. N. Nickel's[20] report on 100 patients at the Henry Ford Hospital, Detroit, the evidence for lupus was well documented, yet over half of the patients were alive at least ten years after the onset of the disease, and of these approximately three-quarters of the men and a quarter of the women were not at all incapacitated. Rupe and Nickel confirmed that symptoms and prognosis were more

severe in the groups with butterfly facial rash, central-nervous-system involvement, or kidney damage, but relatively good in cases presenting additional evidence of rheumatoid arthritis or "post-hepatic cirrhosis." The method of dating prognosis in this study from onset of disease rather than from the date the patient was first seen tends to give a favourable impression, since severe cases of earlier vintage eliminate themselves by dying. Nevertheless, Rupe and Nickel perform a useful service in showing how benign lupus can be. One of their patients is alive after 34 years, and many others are in complete remission.

This problem of spontaneous recovery from lupus (and also from such related diseases as rheumatoid arthritis) is still one of the most mysterious features of the disease. Recovery from infectious diseases necessitates (among other things) the production of antibodies. But how does a patient recover from a disease resulting from the production of auto-antibodies? The fact that recoveries do occur is one of the stronger reasons for supposing that auto-antibodies in lupus are a result, not the cause, of the disease.

WORLD MEDICAL ASSOCIATION

If the national press in this country occasionally confuses the B.M.A. with the G.M.C., it is understandable that the World Medical Association (W.M.A.) should from time to time be mistaken for the World Health Organization (W.H.O.). As medical men themselves seem to be confused about these two international organizations, it would seem necessary to state once again that the World Health Organization is one of the specialized agencies of the United Nations. It is an inter-governmental organization with headquarters in Geneva. One can perhaps best sum up its activities by saying that the W.H.O. is concerned with the public health problems of the world.

The World Medical Association, which met in Berlin last month, is an international organization representing the national medical associations of some 60 countries, is non-governmental, and is concerned at an international level with such professional problems as medical education, medical ethics, and the provision of medical services under social security schemes. It is supported by the subscriptions of its national medical association members, and in addition receives a handsome subvention from a body called the United States Supporting Committee. The W.M.A. operates on a very much smaller scale than the W.H.O., if only for the reason that it has a very much smaller annual budget. Its central office is in New York, and only this year, for the first time in its 14 years of history, has it been possible to employ the secretary-general of the W.M.A. on a whole-time basis.

Much of the work of the W.M.A. has been done in a voluntary capacity by the dozen or so members of the W.M.A. Council working in their spare time. It has, however, consolidated its position as an international medical organization and has close links with such inter-governmental organizations as the World Health Organization and the International Labour Office, before whom it has been able to make effective representations on behalf of the practising doctor. Like so many of its member associations, the W.M.A. throughout the year does a lot of quiet and unobtrusive work which does not bring it to the notice of the public. When the medical profession—for example, in Austria and in Germany—have at different times been engaged in disputes with government and social security organizations, the W.M.A. has been able to offer support and advice, and in particular the advice contained in the principles governing the provision of medical care under social security drawn up in the early years of its existence and elaborated in a document published in 1952.[1] This particular document was prepared as a counterblast to the recommendation of an expert W.H.O. committee that doctors working in social security schemes should be paid on a whole-time basis. The W.M.A. intervened at Geneva and did an effective piece of medico-political work for its member associations.

Perhaps the most outstanding achievement of the W.M.A. was the holding of the First World Conference on Medical Education in 1953 in London, to be followed by the Second Conference on the same subject that took place in Chicago last year, also under the auspices of the W.M.A. The Proceedings of the First Conference provide an invaluable text-book on undergraduate education, and the Proceedings of the Second Conference, now in the course of preparation, should be equally valuable in the field of postgraduate education. If there is one other thing besides education and qualification to practise which distinguishes a profession from other activities, it is an ethical code. Right at the beginning of its existence the W.M.A. drew up an international code of medical ethics, which, with the Declaration of Geneva, has now been adopted by most of its member

[1] *Brit. med. J. Supplement*, 1952, 2, 83.

associations. The W.M.A. in fact made an attempt to bring the Hippocratic Oath up to date. It is hoping to add to this code by drafting a series of rules to guide the medical man in the field of human experimentation. A provisional draft of some of these rules was presented to the General Assembly at Berlin last month, and the discussion that followed showed a widespread interest in this difficult matter. Also at the Berlin meeting there were extensive reports on the cost of medical care in different countries, and a particular interest was shown in the Australian proposal that specially trained health workers should be sent to Papua and New Guinea, similar, so it appeared, to the Russian Feldsher. In the report given to the Assembly it was stated that graduates from the Papuan Medical School, Port Moresby, would not receive a medical degree, but would reach a high enough standard for the duties to be allotted to them. It was interesting to note that this proposal was strongly criticized by medical men from India and Ghana on the basis that nothing should be done to lower the standards of those administering the benefits of modern medicine.

No one could be in West Berlin to-day without being conscious of the political tensions of that beleaguered city. An unfortunate impression somehow grew up during the meeting that the World Medical Association represented "the doctors of the free world." As two at least of its member associations come from totalitarian countries, such an impression is, of course, entirely erroneous. The World Medical Association is weak to the extent that the medical professions of a large number of countries are still not represented in it. And it would be indeed unfortunate, and in the long run completely damaging to the W.M.A., if the idea got abroad, and still more were encouraged, that an international association of medical men and women was allowing itself to be influenced by political ideologies.

THE MIDDLESBROUGH MEETING

Many of the 460 members who attended the third Annual Clinical Meeting of the British Medical Association at Middlesbrough at the end of last week came from far afield. Whether they came as speakers to impart information or as hearers to learn they found, perhaps to their surprise, that this Tees-side industrial town possessed geographical, civic, and human assets which made it an admirable centre for a medical meeting. Chief among the human assets were the enthusiasm, skill, and capacity for hard work of the organizers, ably and energetically led by Mr. J. C. Clark, chairman of the local committee. Supported by Dr. J. B. S. Guy, chairman of the Middlesbrough and Cleveland Division of the B.M.A., Mr. Clark and his keen band of helpers—chief among whom were Dr. J. N. Stirling and Dr. N. K. Smith, honorary general and honorary science secretaries respectively—had arranged a bulging scientific programme and a round of social functions at which the guests, if they had not experienced it already, learnt what a northern welcome really meant.

The centre of the Meeting was the Town Hall, and the reception given there on October 6 by the Mayor, Alderman W. Flynn, and the Corporation of Middlesbrough was a suitable introduction to three days of almost overwhelming hospitality provided by the members of the Middlesbrough and Cleveland Division, by the civic authority, and by Imperial Chemical Industries Ltd.

The Annual Clinical Meetings are not intended to be huge gatherings, and consequently they can provide special opportunities for the participation of the audience in panel discussions and at clinical demonstrations. The latter were admirably arranged at the Middlesbrough General Hospital, the staff of which contributed much to the success of the meeting, for they also occupied the television screen for two hours on Friday morning, tactfully and skilfully compèred by the chairman of the studio panels, Mr. D. C. Dickson, senior surgeon to the North Ormesby Hospital, Middlesbrough. The Tees-side hospitals' School of Radiographers provided charming teams of stewardesses for all the meetings. The Transatlantic clinical conference on endocrinological cases on Saturday evening—the technical arrangements for which were carried out by Smith Kline and French Laboratories Ltd., who also sponsored the television demonstrations—was most enjoyable, but many would have liked to hear more from our strong and eloquent team in Middlesbrough, especially about the American case. The difficulties of fitting what should be a wide-ranging and spontaneous discussion into very strictly defined limits of time have not yet been entirely overcome.

One of the objects of the organizers of the Meeting was to emphasize the importance of industrial health in a town like Middlesbrough, which relies on heavy industry for its prosperity. With the co-operation of the directors of Imperial Chemical Industries Ltd. and Dorman Long and Co. Ltd. visits were paid to the chemical works at Wilton and Billingham and to the Lackenby Steelworks. No

one who saw these vast works in action could have failed to be impressed by the way managements were endeavouring to provide as healthy an environment as possible for their workers. At Wilton, for instance, in the medical centre, which is one of the show places of the works, regular microscopical examination is still made of exfoliated cells from the urinary bladders of workers who have not been exposed to a specific carcinogenic risk for many years.

Mr. Clark and his colleagues at Middlesbrough freely admitted their debt to those who pioneered the annual clinical meetings at Southampton in 1958 and at Norwich last year, but readers of the reports of the proceedings at Middlesbrough in this and next week's *Journal* will see that the Meeting bore a stamp of its own and certainly set a brilliant seal of success on the B.M.A.'s new venture into the clinical field.

HOW MUCH INFLUENZA?

As the falling leaves usher in the season of coughs and colds our thoughts turn again to influenza. What will it have in store for us this winter? Happily there have been no signs so far to suggest that a heavy outbreak is on the way. The difficulties of predicting what to expect from the influenza viruses are well known, but a relatively favourable forecast may be based on the following considerations: there has been no evidence of epidemic influenza in the southern hemisphere during its recent winter (our summer), nor was the disease epidemic in the northern hemisphere in the late spring. Moreover, no antigenically novel virus has recently appeared which could evade the immunity to Asian viruses built up in the last three years. Consequently, though there will almost certainly be some influenza in Great Britain this winter, the chances at present are that there will not be a widespread epidemic. The picture may be confused by outbreaks of respiratory infection due to non-influenzal viruses.

Inoculation against influenza can be a helpful prophylactic, since it probably reduces the chance of getting the disease by about two-thirds. The immunity it confers is unlikely to last more than a year. During the next few weeks to the end of November or into early December is the most appropriate time in which to give the vaccine, and, as was said last year in these columns,[1] the matter is best left to individual choice rather than subjected to a national campaign. Patients for whom influenza constitutes a special hazard might be thought particularly suitable, such as those suffering from severe chronic bronchitis or cardiac insufficiency. Monovalent or bivalent (A2 and B viruses) are preferable to polyvalent vaccines, because unwanted antigen can partly divert the antibody-producing mechanism from making those antibodies needed to combat the epidemic strain of virus.

[1] See *Brit. med. J.*, 1959, 2, 748.

STATUS ANGINOSUS

Cardiac pain due to narrowing of the coronary arteries and myocardial ischaemia is often progressive, starting as pain only on effort and proceeding to pain at rest, or even myocardial infarction, as the coronary arterial disease advances. The term status anginosus has been applied to the clinical state in which there is frequently recurring anginal pain at rest without the electrocardiographic signs of cardiac infarction; though it may end in classical myocardial infarction, this condition may continue as anginal pain for years.

W. F. M. Fulton[1] investigated the coronary circulation in 26 cases of advanced coronary arterial disease by injection of the coronary arteries after death with a radio-opaque medium. Four of these cases were selected for special description: they had in common a long history of relentlessly progressive anginal pain. Pathological examination showed widespread severe coronary arterial disease, narrowing of both coronary ostia, and inner zonal distribution of ischaemic changes in the left ventricle. There was a well-developed arterial anastomotic pattern affecting greatly the subendocardial arterial plexus of the left ventricle. Myocardial damage was in the form of focal necrosis, which was extensive in two cases, and fibrosis in the same distribution. Despite evidence that thrombotic occlusion had been of frequent occurrence, there was no distinct regional infarction. The author postulated that conversion of the coronary circulation into an anastomotic network of dilated channels had removed the anatomical basis on which regional infarction could have occurred.

Recently C. Papp and K. Shirley Smith[2] have studied 20 patients in whom the leading clinical symptom was severe angina at rest, suggesting cardiac infarction, but not followed by the electrocardiographic signs of Q waves, raised R–T segments, or deep T-wave inversion. The series comprised 16 men and 4 women; the ages ranged from 35 to 77 and more than half were over 60. Status anginosus extended over periods lasting from five days to ten months and in many cases developed insidiously from angina of effort. One woman and eight men died. Congestive heart failure was the cause of death in five patients, and in three of these it followed cardiac infarction. In five there was sudden death a few days after cardiac pain.

The dominant electrocardiographic pattern in 14 out of 20 patients was depression of the R–T segment ranging from 2 to 6 mm. in more than two leads, long recognized as a sign of subendocardial ischaemia. In the lateral chest leads the descending limb of R ended well below the P–R segment and continued in a short straight slope downwards and then turned abruptly upward to reach the iso-electric level. This distortion of the S–T segment was seen to a lesser extent in leads I, II, and A.V.L. and was reflected as a raised S–T segment in A.V.R. This change was similar to that found in a positive exercise test for myocardial

[1] Fulton, W. F. M., *Brit. Heart J.*, 1956, **18**, 341.
[2] Papp, C., and Smith, K. S., ibid., 1960, **22**, 259.
[3] Chevalier, H., and Simon, J., *Amer. Heart J.*, 1959, **58**, 120.

ischaemia. These cardiographic features were seen to develop out of the pattern of anterior or posterior cardiac infarction or ischaemia in some cases. In others the electrocardiogram progressed to that of myocardial infarction.

Treatment of this distressing condition is difficult and in many cases unsatisfactory. In some cases spontaneous remission may occur and makes estimates of the value of treatment unreliable. One of the main features of status anginosus is its resistance to all the usual therapeutic measures. Papp and Smith found the euphoric effects of iproniazid or its less toxic homologue nialamide frequently helpful, while long-acting nitrite preparations were of use only in rare instances. Hydrochlorothiazide gave benefit in some cases of nocturnal angina. As an analgesic, pethidine by injection combined with chlorpromazine or promethazine proved to be superior to morphine.

If drug treatment fails, then more heroic measures may have to be tried. H. Chevalier and J. Simon,[3] in an excellent review of the management of angina pectoris, suggest infiltration of the preaortic plexus with procaine or ligation of the internal mammary arteries under local anaesthesia. If the angina is not improved by these methods the creation of therapeutic hypothyroidism by thiouracil derivatives or radioactive iodine may be considered. Surgical methods directed towards revascularization are not without risk and the results are uncertain. Unfortunately this distressing condition is often resistant to all forms of treatment.

ABSENCE OF ONE UMBILICAL ARTERY

An anomaly of the umbilical cord consisting in absence of one umbilical artery has been the subject of several studies in recent years. The observation is not new. Vesalius was the first to describe the anomaly, and an early recorded case is that of C. Bauhin in 1621.[4] Notable reports are those of J. Hyrtl in 1870,[5] K. Benirschke and W. H. Brown in 1955,[6] and Edith Faierman in 1960.[7] The importance of the anomaly lies in its frequent association with other developmental malformations, usually of a serious nature. Benirschke and Brown found other malformations in 76% of 55 cases with a single umbilical artery, and Faierman in 81% of 11 cases. The total incidence of the anomaly is not known. Most of the cords studied have been from dead or malformed foetuses or abnormal placentas, and in these the incidence is certainly higher than in the cords of normal placentas and healthy surviving infants. Faierman found her 11 cases among 411 necropsies.

The associated malformations are various and often multiple. Prominent among them are sympodia or sirenomelia, in which this anomaly of the cord is almost invariably present; acardiac foetuses and other cardiac defects; and maldevelopment of the nervous system, especially anencephaly, and of the genito-urinary system—renal agenesis, urethral valves and atresia, and gonadal dysgenesis. Faierman had two cases of oesophageal atresia. Though many of the associated malformations are incompatible with survival, some are open to surgical correction. If they are internal—for example, oesophageal atresia—the finding of this anomaly of the cord may alert the attendant to the possibility of serious trouble in an infant who is apparently normal at birth. The anomaly is easily detected by a glance at the cut end of the umbilical cord.

[4] Bauhin, C., *Theatrum anatomicum*, 1621, J. T. de Bry (n-p.), p. 40.
[5] Hyrtl, J., *Die Blutgefässe der menschlichen Nachgeburt in normalen und abnormen Verhältnissen*, 1870. Vienna.
[6] Benirschke, K., and Brown, W. H., *Obstet. and Gynec.*, 1955, 6, 399.
[7] Faierman, E., *Arch. Dis. Childh.*, 1960, 35, 285.

TO SLEEP; PERCHANCE TO DREAM

"Ay, there's the rub," said Hamlet. But W. Dement[1] thinks otherwise in an interesting preliminary report on the effects of the forced waking of sleeping subjects. In previous papers[2 3] he has shown that dreaming occurs mainly when the subjects have fast conjugate eye movements and certain electroencephalographic patterns characteristic of light sleep. Such periods of dreaming take place not during the preliminary phase of going to sleep, when the E.E.G. patterns are similar, but only after periods of deeper and presumably dreamless sleep.

In the present study subjects were woken up for several successive nights whenever they began to show these typical eye movements and E.E.G. patterns. Progressively, these people appeared to be dreaming more often, as judged by the increasing number of forced wakenings required on successive nights; they also became anxious and irritable, one even making excuses for not completing the series. These general effects were absent in another series in which the subjects were woken from periods of deep sleep. Dement therefore suggests that a certain amount of dreaming each night is a necessity.

There seem to be other possible interpretations of the data so far available. Perhaps the subjects were dreaming too much and losing deep sleep. The data do not make clear how long they stayed awake after being woken, and it is a common experience that one seems to need some period of deep sleep in order to wake refreshed. But perhaps a person feels he has had a good night merely because his dreams were efficiently preserving sleep, as Freud suggested years ago. Interest in dreams has been revived in psychological circles in recent years, as G. V. Ramsey's article[4] and books by J. A. Hadfield[5] and C. S. Hall[6] attest. Research is beginning to move away from excessive concentration on the latent content of dreams as conceived by Freudians or Jungians. Dement's demonstration of objective evidence for dreaming points to an interesting field for more psychophysiological study.

[1] Dement, W., *Science*, 1960, 131, 1705.
[2] —— *J. nerv. ment. Dis.*, 1955, 122, 263.
[3] —— and Kleitman, N., *Electroenceph. clin. Neurophysiol.*, 1957, 9, 673.
[4] Ramsey, G. V., *Psychol. Bull.*, 1953, 50, 432.
[5] Hadfield, J. A., *Dreams and Nightmares*, 1954, Pelican. London.
[6] Hall, C. S., *The Meaning of Dreams*, 1953, Harper. New York.

We record with regret the death on October 8 of Professor T. B. Johnston, emeritus professor of anatomy at Guy's Hospital Medical School and an editor of nine editions of *Gray's Anatomy*.

B.M.A. ANNUAL CLINICAL MEETING

MIDDLESBROUGH, OCTOBER 6-9

The Association's Third Annual Clinical Meeting was held in Middlesbrough from October 6 to 9. It was a meeting that provided excellent clinical fare and, as would be expected in Yorkshire, most open-handed hospitality. Some 460 doctors, with their ladies, came to it. The gratitude of all is due to Mr. J. C. CLARK, chairman of the local organizing committee, and to his two principal lieutenants, Dr. J. N. STIRLING, the hon. general secretary, and Dr. N. K. SMITH, the hon. science secretary.

On the evening of October 6 a civic reception was given by the Mayor and Corporation of Middlesbrough in the Town Hall. The Mayor and Mayoress, Alderman and Mrs. W. FLYNN, received the guests, and afterwards the Mayor gave a warm welcome to all who had come. Sir ARTHUR PORRITT, President of the Association, in his reply, referred to Middlesbrough's importance as the centre of many industries—steel, pharmaceutical products, and shipping, for example. He then declared the Meeting formally open.

SCIENTIFIC PROCEEDINGS

Friday, October 7

The Scientific Proceedings began on Friday morning with a choice of two major sessions at 9.15 a.m., both well attended. They were a Symposium on Collagen Diseases and Steroid Therapy, and a General Session at which invited speakers discussed "Abdominal Emergencies in Childhood," "The Recrudescence of Venereal Disease," and "Recent Advances in the Treatment of Depression."

SYMPOSIUM ON COLLAGEN DISEASES

Under the chairmanship of Sir ARTHUR PORRITT, this Symposium reviewed the current conceptions about connective-tissue diseases. Sir JOHN RICHARDSON (London) introduced the subject with a general review of the morphology and physiology of connective tissue, which, he pointed out, formed a continuous matrix throughout the body and included bones, cartilages, and the connective tissue of the skin. The three basic elements—cells, fibres, and ground substance—were closely associated with blood vessels, lymph vessels, and nerve fibres. In many connective-tissue diseases it was the vascular disorder which dominated the picture. There were two characteristic cells, fibroblast and mast cells, the former containing granules composed of mucopolysaccharides and proteins, and it might be that these granules were responsible for the development of collagen fibres. The mast cell appeared to be responsible for the storage of heparin and the secretion of hyaluronic acid, and was possibly also concerned with the release of histamine. Its function seemed therefore more related to the ground substance than to the fibres. The ground substance played a very important part in the regulation of water balance, as it was susceptible to changes in hydrogen and other ionic concentrations. It contained proteins from the extracellular fluid and mucopolysaccharides, which varied in quantity and quality in different parts of the body. Changes in its composition might be responsible for the disease states under discussion. The fibres of connective tissue were, respectively, collagenous, elastic, and reticular. The collagen fibres had a specific electron-microscopic appearance. Their width tended to increase with age. It also seemed that collagenase had a greater destructive action on young collagen, which might explain the vulnerability of the collagen in young heart valves in conditions such as rheumatic fever. The ageing process of collagen seemed essentially a drying-out process. Collagen contained over 25% of glycine and had a high content of hydroxyproline and proline. Elastic fibres looked different under the electron microscope, and chemically they contained more valine and less hydroxyproline and proline than collagen. The reticular fibre contained much carbohydrate but had a cross-striation similar to that of collagen. Reticulum might even be derived from collagen, since it had a similar protein constitution.

The essential pathological feature of all the so-called collagen vascular diseases (collagenoses?) was fibrinoid degeneration, but this was not specific, as it also occurred in other conditions such as malignant hypertension and thromboangiitis obliterans. There was increasing evidence that connective-tissue disorders might be manifestations of hypersensitivity, and it was possible that the whole process was an example of an auto-immune reaction. This could be a primary or a secondary factor, but there was as yet no knowledge of the normal protective mechanisms which prevented this occurring universally.

Sir John then summarized Sir Macfarlane Burnet's clonal selection theory. According to this, groups of cells tended to multiply and produce antibody when challenged by an antigen to which they had specific immunological properties. These cells would normally be destroyed and no harm would be done, but if the proliferation got out of hand it resulted in disease. Another theory suggested that the tolerance of the cells to normal antigens was lost by a process of mutation. The support for the auto-immunity theory came from the excess of macromolecules of gammaglobulin in diseases such as rheumatoid arthritis and lupus erythematosus. These molecules were known to contain antibodies. Against the theory were the facts that the level of these factors in the blood did not parallel the clinical course of the disease and their transmission to volunteers did not produce the disease. Normal people could carry these factors in their blood without any clinical manifestations. In spite of these difficulties in accepting the auto-immune theory as the basic cause of these diseases, it was a sobering thought that there existed no other theory to replace it. The association of neoplasms with some of these states could be explained by postulating that the neoplasm produced breakdown products to which cells lost

[*Evening Gazette, Middlesbrough*

Sir Arthur Porritt and the Mayor of Middlesbrough, Alderman W. Flynn, at the Civic Reception on the first evening.

their immunological tolerance. A connective-tissue disease should be suspected under any of the following conditions: (1) When there was pyrexia for which exhaustive investigation had revealed no cause; (2) when a single system seemed to be affected but the disorder was atypical; and (3) where multiple systems were involved, particularly the skin, joints, lungs, blood vessels, and nervous system.

Neural Aspects

Dr. Hugh Garland (Leeds) pointed out that there were more than twenty syndromes covered by the generic title of collagen diseases. In most of them neurological complications could develop, but few presented as primary neurological disorders. Diagnosis could usually only be finally established by biopsy or necropsy. In systemic lupus erythematosus neurological abnormalities were found in 37% of patients, and included convulsions, psychiatric episodes, hemiplegia, aphasia, and frequent changes in the cerebrospinal fluid. Peripheral neuropathy might be symmetrical or assymmetrical, and there might be transient papilloedema and retinal haemorrhages and exudates. The disease seemed to be becoming commoner, but the prognosis was not nearly so gloomy as was previously thought. The L.E. cell was found in 65% of cases and when found had a specificity of 95%. A false-positive Wassermann reaction and negative Kahn reaction occurred in about 25% of cases and were reversible by steroids. The disease responded very well to steroid therapy.

Polyarteritis nodosa resulted in a widespread peripheral neuropathy, but in addition there might be encephalopathy and myelopathy. Furthermore, there was widespread muscle-wasting. On the whole the disease did not respond well to steroids, and specifically the fluoro-containing steroids should not be used because of the risk of increasing muscle-wasting. Temporal arteritis tended to occur in elderly people, and affected both sexes equally. The predominant symptoms were severe headaches and tenderness of the scalp. Ophthalmoplegias and visual defects might also occur, as might a widespread systemic disorder and isolated peripheral nerve palsies. In some cases purpura and polyarthritis ensued. Steroids might prevent the full development of the syndrome but did not cure it once established.

The good response of polymyositis to steroids made it increasingly important to distinguish this condition from genetic muscular dystrophies and carcinomatous myopathies. Very often the diagnosis could be established only by muscle biopsy. The distinguishing clinical features were that polymyositis was usually painful and global. There was no family history. There might be associated dysphagia. Progress was more rapid than in myopathies. There might be an associated skin lesion which histologically could very closely resemble a carcinomatous myopathy. Finally, Dr. Garland discussed the rare condition of thrombotic thrombocytopenic angiopathy. Only 100 examples had been described, although he believed that it might be more common than was generally recognized. It manifested itself as a haemolytic anaemia and purpura, associated with multiple cranial-nerve palsies, which were usually bilateral. He suggested that it might be due to a triple auto-immune reaction affecting platelets, red cells, and small blood vessels.

Pulmonary Aspects

Dr. J. G. Scadding (London) discussed the pulmonary aspects of collagen disorders. He again pointed out that the lungs might be involved in any of the so-called collagen diseases. Thus, in rheumatoid arthritis there might be pleural effusions associated with pleural plaques, plaques which might be histologically specific. Caplan's syndrome was a radiological entity. It was usually symptomless and did not *per se* require treatment. It was caused by exposure of patients suffering from rheumatoid arthritis to coal or many other types of dust: histologically the nodules showed specific rheumatoid changes. It did not respond to steroids. In rheumatoid arthritis one also saw chronic interstitial fibrosis which was indistinguishable histologically from the Hamman–Rich syndrome, the only characteristic feature being the positive Rose–Waaler test in those cases associated with rheumatoid disease.

The pulmonary aspects of polyarteritis nodosa had been clarified by the work of Rose and Spencer,* who had reviewed 111 cases of polyarteritis nodosa of whom 32 had lung changes with certain specific features. In general they found that those with lung lesions alone were the most granulomatous, some even resembling the Wegener granulomatosis. Dr. Scadding pointed out that if one could treat these cases before they had undergone systemic spread they could be controlled, often permanently. Once the systemic spread had occurred, however, steroid therapy was not very helpful. Therefore cases of "intrinsic asthma" occurring for the first time without any obvious explanation should probably be treated with steroids, especially if they were associated with an eosinophilia. In systemic lupus erythematosus the most frequent manifestations were pleural and pericardial effusions. Consolidation of the lung might also occur. Steroids might have to be given indefinitely, but they were not very helpful in the chronic stages of the disease. Systemic sclerosis likewise responded little if at all in the chronic stage to steroid therapy.

Dermatological Aspects

Professor J. T. Ingram (Newcastle upon Tyne), reviewing the dermatological aspects of these diseases, pointed out that the offspring of a woman suffering from systemic lupus erythematosus could itself have all the biochemical and serological manifestations of the disease without any symptoms of ill-health. Usually these manifestations disappeared within six weeks. Most of these diseases as they presented to a dermatologist were specific, and usually there was no tendency for one type of reaction to change into another or to present as a combined syndrome. The effects of climate were obviously very important but little understood. The chronic discoid lupus erythematosus seen by the dermatologist was quite a different disease from the disseminated type of lupus seen by the general physician. Only about 10% of discoid lesions passed into the disseminated phase, but up to 40–50% had laboratory changes suggestive of a systemic spread. The discoid form did not respond to steroids, but was remarkably sensitive to the antimalarial drugs. However, relapse was common, more so than after the old-fashioned treatment with gold salts, which might have a renaissance for this reason. Conversely, in disseminated lupus there might only be skin manifestations in 40–50% of cases. As well as involving the characteristic area of the face, it might affect the hands, and oedema and ulceration of the mucous membranes might occur. Involvement of the scalp with loss of hair was another feature. There was usually a mottled erythema of the palms and soles of the feet, but this was quite a different colour from the lilac discoloration of dermatomyositis. Purpura might also occur, but, according to Professor Ingram's figures, might beneficially influence the course of the disease although seldom curing it. Ten per cent. of patients died within six months, and 80% within four years. On the whole he recommended that steroids should not be used initially unless the patient was seriously ill. Sometimes very good results were obtained with antimalarials alone. The deciding factor was often whether or not there was renal involvement. The various manifestations of systemic lupus could be accurately mimicked by certain drug reactions, such as those caused by aminophylline, mercurial diuretics, and hydrallazine.

Dermatomyositis presented either predominantly as a skin disease or as an early and severe myositis with an incidental skin rash. The lesions were usually lilac-coloured, and there was a general puffiness of the face and a tendency later to form telangiectases and eventually leucodermatous patches rather like radiotherapeutic scars. Eventually ulceration and necrosis might ensue. It was notorious that this condition was often associated with a concealed neoplasm, and the speaker had even seen cases which had

*Rose, G. A., and Spencer, H., *Quart. J. Med.*, 1957, **26**, 43.

recovered despite the progression of the neoplasm. Steroids were not very effective in this disease, and in some cases the use of anabolic hormones was preferable.

GENERAL SESSION

At the general session, held in the Municipal Buildings under the chairmanship of Mr. HAROLD WALKER (Middlesbrough), papers were delivered on abdominal emergencies in children, on venereal disease, and on the modern treatment of depression.

Abdominal Emergencies in Childhood

Mr. J. J. MASON BROWN (Edinburgh) gave an analysis of 1,406 acute abdominal emergencies treated in Edinburgh between 1955 and 1959 with the remarkably low overall mortality of 0.57%, a mortality which was shown on yearly analysis to have progressively declined in that time. He described in more detail problems in diagnosis and the results of treatment of the three common conditions causing abdominal emergencies in children—namely, pyloric stenosis, acute intussusception, and appendicitis. Extremely satisfactory results were now obtained in the surgical treatment of pyloric stenosis in that in the last 10 years 501 operations had been performed with only two deaths, diagnosis being made by palpation of an abdominal tumour at a much earlier stage than previously; the marasmic, dehydrated, poor surgical risk being a thing of the past. Intussusception was the most serious and lethal of the acute abdominal ailments encountered in children and had caused 7 deaths in 265 patients treated. Diagnosis was extremely difficult and consequently often made late. The speaker emphasized that the classic symptom of blood-stained diarrhoea was a late occurrence and absent initially in nearly half the patients studied, while early vomiting, pain, and diarrhoea often caused an incorrect diagnosis of gastro-enteritis to be made. Attempts at reducing the intussusception by barium enema had proved disappointing, the procedure being effective in less than a third of the few patients in which it was tried.

While the mortality from appendicitis had progressively declined in the last 30 years, the diagnosis was often made too late, with a consequent increase in post-operative complications and in the duration of hospitalization. Perforation of the appendix had occurred pre-operatively in two-thirds of children under 5 years and in one-quarter of those between 5 and 11 years. Difficulties in diagnosis were discussed and the clinical differences from mesenteric adenitis described. Only by careful unhurried clinical examination of children, preferably in their own surroundings, could an accurate diagnosis be made, the speaker suggesting some ways in which co-operation between practitioner and surgeon might be improved in the handling of these children.

Recrudescence of Venereal Disease

In producing evidence of the recent recrudescence of venereal disease Dr. C. S. NICOL (London) first reviewed the legal definitions of these diseases, stressing that non-gonococcal urethritis, lymphogranuloma inguinale, and granuloma venereum, conditions occurring with increasing frequency, were not officially included. Ministry of Health returns therefore gave no real indication of the true prevalence of venereal disease. While the annual frequency of syphilis had declined from nearly 24,000 in 1946 to 4,000 in 1958, there had been a recent increase in the number of early infectious cases, especially in homosexuals. Suppression of symptoms and signs by antibiotics might have contributed to this increase and had made diagnosis difficult. Newer specific serological tests for syphilis allowed suspicion to be confirmed in most instances.

The marked increase in gonorrhoea was thought to be related to a big influx of infected immigrants, the emergence of penicillin-resistant organisms, repeated reinfections, and the fact that the disease might cause minimal symptoms in some women, who became reservoirs of infection. The frequency of infections in teenagers was another source of grave concern. Non-gonococcal urethritis had also become increasingly common since it was first notified in 1951. This was an undoubtedly sex-transmitted disease in which infection with *Trichomonas vaginalis* was thought to play a part in approximately 15% of male subjects. Diagnosis was best established by the examination of a urethral smear or of an all-night specimen of urine. Reiter's syndrome, with its associated conjunctivitis, arthritis, sacro-iliac involvement, and skin lesions, was sometimes associated with the urethritis. Promising results had been obtained in patients with this type of urethritis with the new drug metronidazole ("flagyl"), which seemed to cure the majority of patients treated. Lymphogranuloma inguinale and granuloma venereum were sometimes seen in coloured immigrants. In concluding a lecture which had been illustrated by an impressive collection of coloured slides, Dr. Nicol requested that patients be referred to the diagnostic clinic before any treatment was given which might modify the course of the venereal infection.

Treatment of Depression

The striking advances in the treatment of a condition which still produces over 5,000 suicides every year in this country were ably reviewed by Dr. W. W. SARGANT (London). In many of these suicides, depression was reversible by one of the many methods of treatment now available. Often the nature of the depressive illness had passed unrecognized by the attendant physician, there being a real need for expert training of students and practitioners in the multiple and varied symptoms of depressive disease. The development of many new antidepressive drugs in recent years was a major advance in treatment, but too often the extravagant claims made by the manufacturers for a new drug had led to its use in conditions for which it was not suitable. In deep endogenous depression there were no grounds for suggesting that thymoleptic drugs could replace convulsive therapy, though they might by concurrent usage reduce the duration of treatment necessary.

Reactive depression, which produced hysterical and neurotic symptoms in a previously normal personality, was greatly helped by the newer antidepressant drugs phenelzine ("nardil") and isocarboxazide ("marplan"), while aminoxidase inhibitors such as iproniazid ("marsilid") and β-phenylisopropylhydrazine ("cavodil"), although effective, carried the risk of inducing severe hepatic necrosis. Imipramine ("tofranil") was the most effective drug in endogenous depression, and could be used to sustain remissions induced by convulsant treatment. It would seem therefore that many patients with depressive ailments could soon be treated medicinally by the general physician and practitioner, thus releasing the psychiatrist to discover more empirical remedies and to investigate the underlying physiological disturbances in mental illnesses.

COLOUR TELEVISION OF SURGICAL OPERATIONS

After the first two sessions there was a two-hour closed-circuit colour-television demonstration at the Odeon Cinema of surgical operations at Middlesbrough General Hospital. The technical arrangements were sponsored by Messrs. Smith Kline and French Laboratories Ltd. Mr. J. C. CLARK (Middlesbrough) acted as moderator for this successful programme, which was divided into four parts. Mr. D. C. DICKSON (Middlesbrough) acted as chairman of the panel throughout the programme. Dr. A. K. LAMBALLE was the television liaison officer. The first discussion was devoted to hallux valgus.

Mr. G. PARKER (Middlesbrough) performed an impressive and well-presented Keller's operation. The stages of the operation—extensor hallucis tenotomy, excision of the base of the proximal phalanx with the fashioning of a flap of tissue to cover its raw stump, trimming of the osteophytes at the head of the first metatarsal, and excision of the bunion—were all clearly seen. Mr. M. D. LEITCH (Middlesbrough) presented a clear exposition, using models, of the rationale

of the operation, and explained current ideas on methods of treatment and aetiology. Dr. A. K. LAMBALLE (Middlesbrough) described the radiological features of hallux valgus, and Mr. PARKER expressed a firm opinion that the wearing of pointed shoes was only of subsidiary importance in the development of this condition.

Next Mr. S. MOTTERSHEAD (Middlesbrough) gave a witty and very clear demonstration of the operation for repair of femoral hernia which was devised by the late P. G. McEvedy. This operation could easily be followed because of the clear diagrams which were presented in the studio by Mr. G. E. FORDYCE (Middlesbrough). Dr. J. W. RIDLEY (South Bank) made plain the helpful attitude of the industrial medical officer concerned with rehabilitation of the patient who had recently undergone herniorrhaphy. The advantages of the McEvedy approach—good exposure with opportunity to deal with any complications—were stressed. In answer to a question, Mr. MOTTERSHEAD gave his opinion that any surgeon who adopted this technique would soon prefer it to all others.

As the third item, Mr. B. H. ELLIS (Middlesbrough) gave a demonstration of a total abdominal hysterectomy for a large uterine fibroid. The stages of the operation could easily be followed. The panel explained that total hysterectomy removed the risk of malignant disease of the uterine cervix, but for technical reasons it was occasionally advisable to leave the cervix *in situ*. The possibility of myomectomy for uterine fibroid was discussed; it was concluded that it had its place in the treatment of the younger female who still hoped to enlarge her family. Mr. ELLIS gave due credit to the ease of access which modern anaesthetic techniques allowed. In answer to a question he stated that he prescribed stilboestrol for the patient under 45 years in whom both ovaries had to be sacrificed. Dr. W. M. MORGAN (Saltburn-by-the-Sea) made some useful observations on the place of the family doctor in the aftercare of these patients.

The final item was marred technically by difficulties in the operating-room, but these did not occur before Mr. J. POTTER (Stockton-on-Tees) had had the opportunity to explain the plan and purpose of the secondary operation for harelip and cleft palate which he was performing. Dr. JOHN J. TILLIE (Middlesbrough) underlined that team-work was necessary in the management of these cases, and described the vital job of the paediatrician in neonatal care. These patients should be admitted to hospital. The first operation usually took place at age 10–12 weeks; the next followed at roughly one year, and final adjustments were made at about two years. Mr. J. T. COOK (Middlesbrough) explained, and illustrated clearly with the aid of casts, the necessity for an orthodontist to form part of the therapeutic team. Finally, we were shown briefly two young boys who had previously been operated upon with very satisfactory results.

PANEL ON ANTENATAL CARE

On Friday afternoon there were two consecutive Panel Discussions. The title of the first was "Antenatal Care: Can it be Overdone?" The chairman was Dr. A. MORRISON (Darlington) and the panel consisted of Dr. J. C. ARTHUR (Gateshead), Miss JOSEPHINE BARNES (London), and Dr. JEAN MACKINTOSH (Birmingham).

Dr. ARTHUR said that a decrease in maternal mortality had resulted from a number of factors, of which antenatal care was one of the most important. The care must, of course, be tailored to suit the individual patient, for obviously some women would require more attention than others. Miss BARNES pointed out that the usually accepted minimal standards applied to the normal case, but the others would naturally need a much more flexible arrangement. Some women might require to be seen more often than weekly, and indeed there was need for a greater provision of antenatal beds. Dr. JEAN MACKINTOSH said that the figures for the stillbirth rate and mortality during the first week of life were still poor, and she thought that with good antenatal care these figures could be halved.

Fear of the patient becoming overdependent on the doctor was dismissed by all the members of the panel because most doctors realized the need to handle people as individuals. The danger of too many vaginal examinations in pregnancy was raised by one of the audience, but Miss BARNES pointed out that there was no danger in a vaginal examination carried out before the 36th week of pregnancy, provided care was taken to ensure that the glove-finger was satisfactorily sterilized. She emphasized the risk of monilia infection when this precaution was omitted. Many of the audience were interested to know what the panel thought about the question of where the babies should be born, and the general conclusion appeared to favour having the first child, at any rate, in hospital and subsequent children at home or in hospital, according to circumstances. Reference was also made to the changing emphasis in antenatal care. Dr. ARTHUR pointed out that 30 years ago the emphasis was anatomical, on the dimensions of the pelvis. Nowadays the great emphasis was on the prevention and detection of toxaemia. He alluded to the help that the local authority could give, for example, in facilitating the performance of blood examinations, and also in providing ancillary services such as motherhood classes and a dietetic service. Miss BARNES thought that the change in emphasis affected not only the doctors, who had become more "antenatal-care-conscious," but also the public, who as a result of magazines were also becoming more "care"-conscious. On the differential diagnosis between pre-eclamptic toxaemia and mild essential hypertension, Miss BARNES said that the diagnosis depended on the blood-pressure recording made when the patient was first seen, which was usually in the first three months of pregnancy. In eclampsia the blood-pressure rose only after the 20th week, whereas in essential hypertension the pressure was initially raised, so that the general practitioner was in a good position to make the diagnosis from his previous knowledge of the patient. Reference was also made to the greater importance of the diastolic than the systolic pressure, and the need to bear in mind differences between antenatal hypertension and ordinary "medical" hypertension, since most cardiologists disregarded those mild rises in pressure which were viewed with such apprehension by the obstetrician. The importance of recognizing the drop in blood-pressure that commonly occurred around the middle of pregnancy was stressed. In all events a *rising* blood-pressure was to be regarded as more serious than a raised blood-pressure.

There was general agreement that in this country we were behind the Australians and New Zealanders in some aspects of antenatal care. This was attributed to their closer supervision of diet in pregnancy and to their prompt attention to any antenatal abnormality. Dr. ARTHUR and Miss BARNES emphasized the necessity of seeing each woman after the 28th week at intervals of two weeks and then of one week. There seemed to be general agreement on the value of some form of education in relaxation, and this was taken to include the very important matter of ensuring the confidence and mental relaxation of the patient, in particular if she was a nervous young primipara. The panel held that dietary restriction for undue gain in weight should not be supported by the use of appetite-suppressing drugs such as dexamphetamine. The haemoglobin should be measured when the patient was first seen, but if iron was indicated it should, as far as possible, be withheld until after the nausea of early pregnancy had passed off at the end of about the third month. It was generally satisfactory to start oral iron therapy at the 20th week. Dr. LENNOX M. JOHNSTON (Wallasey) wondered if smoking was bad for the mother or infant, since there had been a report that mothers who smoked produced babies that were slightly smaller than those who did not. The panel, however, thought there was no special indication to make the mothers stop smoking, since there was little evidence that it was harmful to foetus or parent and it did not seem to affect breast-feeding at all. On the contrary, the mental relaxation from a cigarette was thought to be beneficial. One general practitioner emphasized the superiority of having antenatal care

supervised by the doctor himself rather than the hospital, for this, he thought, would ensure the preservation of the personal relationship with the patient and also continuity throughout the whole period of pregnancy, puerperium, and afterwards. In conclusion the chairman, Dr. MORRISON, summed up the feelings of the panel that antenatal care was not being, and indeed could not be, overdone. Instead, there was evidence that some aspects of it were in fact being underdone.

PANEL ON BACKACHE

Under the chairmanship of Dr. J. B. S. GUY (Loftus) there was a lively panel discussion on "Backache." This was in the form of questions submitted previously by members of the audience. The first asked the commonest cause of low backache in the young housewife. Mr. H. OSMOND-CLARKE (London) believed that, if some strains could be excluded, the cause was most commonly to be found in an habitually flexed posture—indeed, he agreed strongly with a comment from the floor that a low sink or ironing-board was a causative factor. As Professor H. HARVEY EVERS (Newcastle upon Tyne) stressed, the age and parity of the patient must always be regarded in considering the possible cause. Because pelvic infection was now very rarely seen, "gynaecological" backache was uncommon. He felt that backache referred from the pelvic organs was always associated with descent of the uterus, leading to traction of the ligaments, or alternatively it was a symptom of underlying malignant disease. Dr. J. CYRIAX (London) mentioned that pain referred from the pelvic organs did not interfere with movements of the back, and he regarded this as an important diagnostic point. Dr. Cyriax went on to comment on the part played by the lithotomy position, by bed rest, and by all the young mother's chores in running a house and looking after a baby in causing lumbar flexion, and hence encouraging a prolapse of a lumbar intervertebral disk. In answer to further questions from the floor, Professor EVERS pointed out that pain referred from the pelvic viscera was relieved by lying down, whereas pain from malignant disease was continuous.

The next question asked for advice on the best treatment for the family doctor to prescribe in low backache. Dr. CYRIAX strongly recommended manipulation *without* anaesthesia. If the diagnosis was correct there was no reasonable danger from this manœuvre. He believed that prolapsed disks were reduced by this means, and that after reduction the patient should be carefully advised to avoid flexion and to maintain a posture of lordosis. Mr. OSMOND-CLARKE agreed with this, but took the opportunity to stress the great danger of producing massive disk prolapse and a complete chorda equina lesion by manipulation under anaesthesia. Apart from manipulation he believed strongly in a period of rest on a firm mattress, and then advised exercises (with lumbar flexion excluded) and the wearing of a corset. Professor EVERS stressed the importance of a very careful and complete history and physical examination (including pelvic and rectal examination) before proceeding to treat back pain. Only in this way could one avoid overlooking unsuspected malignant disease. His colleagues on the panel agreed strongly with him. Questions from the floor raised the possibility of muscular hypotonia as a contributory cause of prolapse, and inquired into the type of personality of the typical patient suffering from backache. Regarding hypotonia, it was agreed that this either played no part or only a subsidiary role; many young, powerfully built males suffered from prolapsed disks. Regarding the personality of the patient, Dr. CYRIAX thought most of them to be average, whilst a few had a low threshold for pain, and a few had discovered that backache was a symptom which medical attendants could not disprove.

The final question asked advice on the different methods of treatment. Dr. CYRIAX and Mr. OSMOND-CLARKE answered jointly. The place of traction, bed rest, epidural analgesia, and the wearing of a corset were all discussed. Both speakers endorsed the value of epidural analgesia. Mr. OSMOND-CLARKE explained that fewer patients underwent exploration nowadays. He believed that operation was indicated for (*a*) very severe pain; (*b*) repeated attacks; and (*c*) continued chronic pain which prevented a normal way of life. He described the limited place of spinal fusion. In answer to questions from the floor, Mr. Osmond-Clarke believed that the coal-face worker with a prolapsed disk might never return to his original heavy work. Whatever his treatment, his back was abnormal. The questions from the floor indicated the interest of the audience, and it was with reluctance that the chairman closed the proceedings.

MEDICAL FILMS

The last scientific item on Friday was a programme of medical films. There were two films. The first was a silent colour film made by the Photographic Department of University College Hospital. It illustrated the indications for and the technique of pudendal nerve blocks. The application of pudendal block in low forceps delivery in the third stage of labour was shown in detail. The anatomy of the pudendal nerve arising from the second, third, and fourth sacral segments, coursing around the sacro-spinalis ligament and through Alcock's canal, was demonstrated on models. The surface markings enabling a simple approach to be made were outlined. The photography throughout was excellent.

The second film, made by Stanley Schofield Productions, Ltd., took the form of an illustrated lecture by Dr. H. M. Sinclair, of Oxford. He presented cogent arguments in favour of the theory that the current increase in atherosclerosis and coronary heart disease was attributable to changes in dietary habits. Most of the relevant changes concerned the dietary fats, and were due in part to modern methods of animal feeding and in part to the practice of hydrogenating fats before selling them to the housewife. This made them more elegant in presentation and easier to preserve, but it did alter the ratio of essential to non-essential fatty acids, which led to failure of esterification of the cholesterol. The latter then collected in the blood plasma, and was eventually laid down in the intima of blood vessels as atheromatous plaques. The arguments against accepting the theories of stress and lack of exercise as a cause of arterial degeneration were presented and possible prophylactic measures were discussed. Nicotinic acid and oestrogens were theoretically useful, but had practical disadvantages, and anticoagulants were often illogical, as often the cardiac infarct was not due to a thrombosis. The only reasonable approach was to give essential fatty acids in the form of vegetable oils, but these were unpalatable in the doses in which they would have to be taken to be effective. It was, however, now possible to give lecithin together with pyridoxine in capsule form, and this would achieve the same result. To illustrate this in a most impressive way, the serum of the lecturer, who had taken lecithin after a meal with a high content of animal fat, was compared with that of a control who had eaten an identical meal. The contrasting appearances were most striking, and suggested that here indeed was a subject worthy of even more intensive research. The photography and production were of a very high standard.

This report will be concluded next week.

As a result of a request from the Ministry of Health, a new British Standard (B.S. 3271:1960) for surgical elastic band trusses has been published. It specifies requirements for materials used in the manufacture of component parts of elastic band trusses, together with such dimensions as are independent of the individual clinical requirements. Provision is made for inguinal and scrotal elastic band trusses with fixed pads or adjustable pads (excluding sliding pads). Copies of this standard may be obtained from the B.S.I., Sales Branch, 2 Park Street, London W.1, price 5s., postage extra to non-subscribers.

NEW ACADEMIC YEAR

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

In presenting his report for 1959–60 at the inaugural session of King's College Hospital Medical School on September 30, the Dean, Dr. VERNON HALL, said the erection by the Board of Governors of a new ward block of 80 or more additional beds would enable professorial units in medicine and surgery and a unit in obstetrics and gynaecology to be created. Plans had already also been submitted for the erection of a new animal house, and a new hostel for about 50 medical students was envisaged adjacent to the hospital.

Opportunities in Africa

Lord TWINING, a former Governor of Tanganyika, delivered the inaugural address. He spoke of medical work in Africa. The first thorough-going medical policies there had been initiated during and after the first world war. The general principle had been that each district headquarters should have a reasonably well equipped hospital staffed with European doctors and nursing sisters, with health centres at selected points and sub-dispensaries each in charge of African staff and subject to visits by the medical officer. Originally no charge was made for medical treatment except injections, but as the demand for injections was enormous the local Governments had taken the initiative and raised local taxation in order to pay for the medical services. To-day, the whole area of the East African Territories was covered with a network of well-equipped hospitals, health centres, and dispensaries. In addition there were various institutions for specialist treatment, such as tuberculosis hospitals and leper settlements. It was very difficult, he said, to strike a balance in the demands for improved facilities. Certain conditions, such as blindness and leprosy, had a strong emotional appeal to the public, who constantly demanded that the Government should divert funds to these specialist purposes which were urgently wanted for general medical work.

There were quite a number of Africans who had natural talents for medical work, but unfortunately the cost of training African medical officers was very high and the number of candidates who reached a general educational standard and were willing to undergo a long period of training was few. At present the medical school at Makerere was unable to turn out more than 15 doctors a year. "Therefore," said Lord Twining, "the need for expatriate medical officers is still very real and is likely to remain so for many years to come." He referred to the following figures as illustrating the position: In West Germany the proportion of doctors to population was 1 to 490; in Soviet Russia 1 to 600; in the United States 1 to 790; in the United Kingdom 1 to 900; in Kenya 1 to 12,000; in Uganda 1 to 18,000; in Tanganyika 1 to 22,000; and in Ghana 1 to 25,000. Each of the three East African Territories had about 150 expatriate medical officers, and when independence was attained it was likely that some would elect to return to Britain. This would be an anxious problem, because they would be needed more than ever before. Lord Twining continued: "I believe that in this neo-Elizabethan period the spirit of adventure in this country is as high as ever, and that, with the right conditions, there would be no lack of medical men from this country willing, and even anxious, to serve in backward countries overseas." Professional men, particularly doctors, had much greater scope for their skill and for gaining experience in African countries than they would have at home. When independence was gained, Great Britain should offer a helping hand by continuing to provide facilities for postgraduate and specialist training. He ended by saying: "I commend to you, particularly to you medical students, the idea of taking your medical skill to these countries where it is needed so much."

FACULTY OF MEDICINE, BIRMINGHAM UNIVERSITY

Mr. L. FARRER-BROWN, director of the Nuffield Foundation, gave the address at the inauguration ceremony of the Faculty of Medicine, Birmingham University, on October 3. The title of his address was "Acting on Probabilities." He said that he had been influenced in his choice of subject by a recent letter in the press which had suggested that it was time to "destroy the myth" that Sir Francis Drake had been playing bowls when the Spanish Armada approached. It was the phrase "Let us destroy the myth" which had triggered off his decision to speculate on the relation between knowledge and the ability to use knowledge well. It was the seeking and assimilation of what were described as "the relevant facts," and the bearing of this process on the forming of judgments, that interested him.

Judgment in Hospital Planning

Whether or not the talent of "guessing right" was the king of talents, it was of great importance in human affairs. Because it was an unreliable skill, and one which could scarcely be taught, one might ask how much point there was in trying to make as accurate and complete as possible the information upon which such frail judgments were based. One might perhaps arrive at an answer by looking at the practices of men adept in reaching decisions in fields in which they were experts, and Mr. Farrer-Brown took as his examples the ancient and learned professions of the law and medicine, interposing between them the craft of grant-giving.

Turning to the decisions reached by people outside the realm of their own expertise, Mr. Farrer-Brown suggested that, if he might be allowed one rash generalization, "the greater our ignorance of such relevant facts as exist the more dogmatically assertive our judgments become." If it were true that the more civilized we became the more relatively ignorant we were bound to be of the working of our civilization, the upshot must be, to some extent, dependence on the expert. But the layman need not always accept blindly the expert's conclusions; he could at least attempt to test the evidence. Musing on the strange state of affairs which would come about were it forbidden to make a pronouncement without stating the nature of the supporting evidence, Mr. Farrer-Brown suggested that it would be all to the good if, in matters outside their specialist spheres, men adopted the same attitude to the evidence as they did within those spheres. He pleaded for the adoption of such an attitude to hospital planning. The architects involved were showing commendable enterprise in striving to assimilate all that was known, but the crucial decisions remained the responsibility of the medical and nursing professions. If they were as well informed as they should be, if they were assembling and evaluating the relevant information as they would in reaching a clinical decision, it would help immensely towards an understanding of what were the client's true needs, and of the environment in which medicine could be practised at its finest.

WESTMINSTER MEDICAL SCHOOL

The Dean of Westminster, Canon E. S. ABBOTT, delivered the inaugural address to the Westminster Medical School on October 3. Addressing himself to the students, Canon Abbott said that an image of the good doctor had been handed down, and he hoped that in entering the great and honourable profession of medicine they would not too impatiently reject that image which still remained in the public's mind.

Image of the Good Doctor

It was the image of someone who was more than a technician. On the other hand, it was the image of someone who was much more than merely kind. The bedside manner was no doubt very helpful, but it was to be hoped that the doctor would pride himself on his practicality and keep himself up to date. It was, in fact, the image of someone who combined high scientific skill with a strong spirit of vocation. The general public recognized that every doctor had to undergo a very long and very exacting training. The outstandingly successful doctor was rarely able to achieve his eminence by any other means than those of exceptional ability and disciplined application under the

constant eye of intensely critical colleagues. The image of the good doctor was that of a man or woman who, while understanding the patient's physiological and psychological make-up and his social and economic environment, was also prepared to deal with the patient in his mysterious, personal uniqueness.

In the modern moral and spiritual confusion of to-day, many people who failed to find happiness from their own resources came to the doctor looking for help and guidance. That help and guidance could not be found on the medical level alone, but those people were prepared to accept it from a doctor and not from a priest or a moralist, because the doctor had a reputation for being a realist upon whose practical judgment they could rely. For that reason alone, the general practitioner could not be a mere technician. He found himself compelled to exercise a kind of pastoral office for which often he might feel himself untrained, and for the fully responsible exercise of which he certainly had not the time.

As the profession of medicine was to-day at one of the great turning-points in its history, it was infinitely desirable, said Canon Abbott, that medical students should have an adequate doctrine of man as a being who, although he was part and parcel of creation and physically died, also transcended the creation of which he was a part—as a being who belonged to two worlds at once, the outward world of sense and the spiritual world which Christians would say was eternal.

THROMBOSIS AND ANTICOAGULANTS

SYMPOSIUM AT DUNDEE

[FROM SPECIAL CORRESPONDENTS]

A symposium on thrombosis and anticoagulant therapy was held at Queen's College, Dundee, from September 28 to October 1. Amongst the fifty members of the symposium were distinguished guests from overseas and from the United Kingdom. The excellent arrangements for the meeting were made jointly by Professor P. A. OWREN, of Oslo, and by Professor R. B. HUNTER and Dr. W. WALKER, of Dundee.

Current Concepts of Blood Coagulation

The first session, devoted to current concepts of blood coagulation in relation to vascular disease, was held under the chairmanship of Professor Sir GEORGE PICKERING. It soon became apparent that there are large gaps in our knowledge of the relationship between coagulation, thrombosis, platelets, atheroma, fats, fibrinolysis, and sudden death. Dr. J. R. A. MITCHELL (Oxford), in giving an appraisal of thrombosis, blood coagulation, and atheroma, stressed that thrombosis was not synonymous with intravascular clotting. A blood clot had a homogeneous structure, the blood components being evenly distributed in a fine mesh of fibrin. A thrombus, however, was not homogeneous. There was a paucity of red cells, and microscopical examination revealed selective deposition of fibrin and some cellular material, indeterminate areas being scattered throughout the section. The relationship between general atheroma, coronary atheroma, coronary thrombosis, and myocardial infarction was not clear. Indeed, we did not know whether we were dealing, in myocardial infarction, with a disease that was primarily of the vessel walls or one that first affected the constituents of the blood. Dr. M. MATTER (Zurich) stressed the fact that we were ignorant of the importance of an increase in the amount of any blood coagulation factor prior to thrombosis. Thromboelastography was valuable in investigating the importance of this aspect of the problem, but at present only as an academic exercise. Serum entering the circulation after trauma might aggravate a clotting tendency.

Dr. J. C. F. POOLE (Oxford) gave an interesting description of the solid body that develops in blood when it is allowed to flow round a closed circular loop of plastic tubing. This was similar to a thrombus rather than to a clot. With human blood, heparin much reduced the "red tail" of this thrombus without affecting its "white head." The time required for the thrombus to form was shortened by long-chain saturated fatty acids, but not by short-chain fatty acids or by unsaturated fatty acids. Professor H. W. FULLERTON (Aberdeen) had used the recalcified plasma clotting time to measure blood coagulability. This R.P.C. time was accelerated by a fatty meal when in-patients were studied, but the acceleration of clotting was less with out-patients or "sedentary" students, and there was practically no acceleration following a fatty meal in active students. This might support the view that there was an increased tendency to thrombosis in patients at rest in bed. The acceleration of the R.P.C. time did not occur in in-patients or out-patients under treatment with phenindione. Dr. S. NIEWIAROWSKI (Warsaw) delivered, on behalf of Professor E. KOWALSKI, a paper dealing with interrelationships between thrombosis, coagulation, and fibrinolysis. Hageman factor appears to be important in the initiation of both blood coagulation and fibrinolysis. Dicoumarol drugs inhibited fibrinolysis, but heparin did not. If treatment with proteolytic enzymes was attempted, antithrombins would be released and might lead to a haemorrhagic diathesis.

Dr. A. S. TODD (Dundee) described the technique of fibrinolysis autography, and members of the symposium were most impressed by its possible applications and by the results already obtained. A tissue activator of plasminogen was found in endothelial cells, particularly in veins. Less active cells derived from arteries appeared to contain a precursor of plasminogen activator. Thrombosed vessels showed endothelial activity only in those areas where the thrombus was not firmly adherent, and this might be a factor in the adhesion of a thrombus to the vessel wall.

Control of Anticoagulant Therapy

Sir JAMES LEARMONTH was the chairman of a session dealing with the organization and laboratory control of anticoagulant therapy.

Professor P. A. OWREN (Oslo) considered that the highest priority for long-term anticoagulant therapy should be given to patients in the following groups: (*a*) Chronic rheumatic heart disease with recurrent thrombo-embolic episodes. (This included, especially, old people, those with a large left atrium, and those with atrial fibrillation.) (*b*) Angina of less than two years' duration. (*c*) Myocardial infarction (one episode and angina for less than two years). (*d*) Atherosclerosis in the legs without evidence of coronary thrombosis or cerebral thrombosis. (*e*) Intermittent insufficiency of the cerebral circulation. (*f*) Retinal thrombosis. Second priority should be given to those with: (*a*) Rheumatic heart disease without thrombo-embolic episodes. (*b*) Angina for more than two years. (*c*) Two or more myocardial infarcts. This would result in anticoagulant therapy being required for 0.2 to 1% of the population. For management the "thrombotest" on capillary blood had distinct advantages.

Dr. H. HARTERT (Heidelberg) formerly carried out the routine control of anticoagulant therapy with coumarin drugs by thromboelastography, using recalcified citrated blood, but had found that the use of oxalated blood increased the sensitivity of the test for demonstrating a thrombosing tendency. However, the method was not satisfactory for demonstrating a *bleeding* tendency, and it seemed that at present two tests might be required to control anticoagulant therapy—one for the thrombosing tendency and another to assess the danger of bleeding. Dr. W. ZOLLINGER (Zurich) had carried out a detailed study of the value, in the control of anticoagulant therapy, of tests using human brain thromboplastin, thrombokinase (Geigy), thromboplastin (Roche), and Owren's thrombotest. The two simplest tests were the one involving thrombokinase (Geigy) and the thrombotest. Both could be used with capillary blood. Unlike some other workers, Dr. Zollinger did not find that

the thrombotest was sensitive for factor IX deficiency, and the Geigy thrombokinase had the disadvantage at the commencement of anticoagulant therapy of being insensitive to factor VII depletion. For any of the tests, the instructions must be followed exactly.

Dr. W. WALKER (Dundee) considered that the prothrombin and proconvertin test (P and P test) was more sensitive and probably better than Quick's test, but it was not suitable for carrying out large numbers of investigations in routine laboratories. Teething troubles with the thrombotest had been overcome, and this was now the method of choice for long-term anticoagulant control on out-patients, capillary blood being used. At present the reagents were expensive, but the advantages outweighed this cost. For in-patients and for samples of blood sent by post, Quick's method should be used, unless all contact with glass could be avoided, when the thrombotest was possible.

Myocardial Infarction and Peripheral Vascular Disease

On the second day there were sessions dealing with the use of anticoagulants in the prophylaxis and treatment of disease, and with heparinoids and their place in therapy. The chairmen were Professors I. G. W. HILL and P. A. OWREN.

Professor R. B. HUNTER (Dundee) reviewed the way in which our knowledge of the practical value of anticoagulant therapy had developed. In the M.R.C. trials, long-term therapy with coumarins and related drugs in myocardial infarction had shown results to be best in males aged 45 to 54 receiving a high dosage of the drugs. He wondered whether lifelong therapy should be given to all patients after myocardial infarction, or with angina of effort. Further controlled trials were necessary, particular attention being paid to unfortunate incidents that might arise if anticoagulant therapy were stopped. Dr. R. L. RICHARDS (Glasgow) analysed the results of a clinicopathological study of 446 cases of acute myocardial infarction admitted to one medical unit over a period of 11 years. He excluded 59 patients who died within 24 hours; he then had 63 deaths from 302 patients given anticoagulants, and 29 deaths from 85 patients not receiving them. Of those who died, there was a lower incidence of thrombo-embolic manifestations, intracardiac mural thrombus formation, recent coronary thrombosis, pulmonary infarction, or systemic infarction in patients who had received anticoagulants. Haemorrhagic phenomena and (strangely) rupture of the heart were not a feature where anticoagulants had *not* been given, but of the 52 necropsies in the group who *had* received anticoagulants cardiac rupture was found in five and haemorrhagic features in eight. The latter was not related to overdosage of anticoagulants.

Mr. G. SMITH (Glasgow) dealt with anticoagulant therapy in peripheral vascular disease. Without anticoagulant therapy, of 58 cases seen in five years on account of thrombo-embolic phenomena in peripheral vessels 17 had died, 27 were unchanged or improved, and 14 were worse. There was evidence of general vascular disease in 31 of the survivors. In discussing the value of endarterectomy, Mr. Smith outlined a scheme in which this was done under cover of heparin, and followed by phenindione as long-term therapy. The operation had been carried out in 16 patients with isolated lesions in the femoral or popliteal arteries. After a year one had died and another reoccluded. When the operation was done on 16 patients with severe generalized atherosclerosis, one had died after a year, and four had required operation for gangrene. Ten patients with thromboangiitis obliterans had been treated with phenindione for a mean of five years. No major amputations had been necessary. Good results had been obtained from treating digital arterial occlusion of the hands with heparin. Dr. M. J. LARRIEU (Paris) had used "coumadin" prophylactically in 32 patients undergoing orthopaedic operations. The inital dosage varied from 1.5 to 12.5 mg., and maintenance dosage from 2.5 to 10 mg. There had been no thrombo-embolic episodes, but haemorrhage occurred in three patients.

Pulmonary Embolism

Dr. A. C. TURNBULL (Dundee) stated that pulmonary embolism was the most important cause of mortality after gynaecological surgery. Often there was no clinical evidence of venous thrombosis before embolism occurred. He had carried out a trial of phenindione prophylaxis given until the 12th post-operative day in 200 patients undergoing surgery for gynaecological reasons. There was a significant absence of pulmonary embolism, compared with four episodes in 220 controls. Although bleeding occurred in 23% of the treated group as compared with 12% of controls, severe haemorrhage was exceptional. Bleeding occurred particularly after colporrhaphy. Between 1951 and 1954, among 1,271 gynaecological operations without anticoagulant cover 50 thrombo-embolic episodes occurred: there was a fatal outcome in 8. From 1957 to 1959 there had been pursued a policy of giving phenindione to patients in whom there appeared to be a risk of thrombo-embolic episodes. Of the 370 patients so treated only one had such an episode after operation, while of the 465 not treated 12 had had thrombo-embolic complications, a fatality occurring in one. After gynaecological operations, death from pulmonary embolism was likely, without anticoagulants, only in those over 45 years who were overweight, or in those with a previous history of thrombo-embolism, and this had been the basis for selecting patients for prophylactic anticoagulants.

Cerebral Infarction

Dr. A. BARHAM CARTER (London) discussed the use of anticoagulants in the treatment of cerebral infarction. Of 478 males and 524 females admitted to Ashford Hospital between 1952 and 1958 for cerebral accidents, 85 had embolism, 425 thrombosis, and 492 haemorrhage. In recent years the incidence of cerebral embolism from mitral stenosis had diminished, while that from myocardial infarction had increased. Anticoagulants should be given in cerebral embolism. Of 257 cases with cerebral thrombosis, 76 seemed suitable for a controlled trial with anticoagulants, half of these being given the drug. Although 26 patients in the treated group had recovered or improved, this was not significantly better than in the controls. However, if cases with incomplete lesions were selected the evidence for the value of anticoagulant therapy was greater. Long-term therapy had been tried in 16 patients and the results compared with those in 16 controls, and, although the groups were small, the results were encouraging. Anticoagulants should not be used in cerebral infarction if there was persistent hypertension, blood in the C.S.F., age over 70, or a history of peptic ulcer, gastro-intestinal haemorrhage, or hepatic disease. They should not be used routinely for clinical cerebral infarction.

Dr. J. MARSHALL (London) regretted that there was nothing comparable to the electrocardiograph for the investigation of suspected cerebral thrombosis. He had carried out the statistical analysis of the results of his trials by sequential analysis. The "acute" trial consisted of giving heparin, followed by phenindione, and maintaining prothrombin levels by Quick's method at 2–3 times normal, to 50 patients under the age of 70 with non-embolic cerebral infarction. They had been treated within 72 hours of onset, and there was no evidence of any benefit. The "long-term" trial was on patients under the age of 70, seen at least 14 days from the last accident, which was again non-embolic. The prothrombin time was kept at 2–2½ times normal. There were 71 cases and 71 controls and the trial lasted 21 months. No benefit ensued. Possibly the trouble was that it was impossible to know which patients had cerebral haemorrhage of a minor degree and which had cerebral thrombosis.

New Anticoagulants

After Dr. S. NIEWIAROWSKI (Warsaw) had reported studies of the mechanism of the anticoagulant action of

heparin, Dr. F. K. BELLER (Tübingen) discussed the heparinoids. Most were unsuitable for clinical use because of their toxic effects, which included tachycardia, nausea, vomiting, cyanosis, and alopecia. He described, however, trials of a more satisfactory heparinoid, Geigy G31150, which had more anticoagulant activity than any of the analogues hitherto tried, and much less toxicity. It was cheaper than heparin and might perhaps be used to supplement it in therapy.

Dr. E. WINDSOR (California) described experiments with sulphopolyglucin (SPG) in dogs. Its oral absorption was increased by the addition of an alkali salt of ethylene diamine tetra-acetic acid. Its anticoagulant effects were similar to those of heparin, but there was with SPG a dose-dependent difference in lipaemia-clearing activity in that a delay in lipaemia clearing occurred when doses were given intravenously. Protamine sulphate prevented or terminated both antilipaemic and anticoagulant effects of SPG. Dr. W. WALKER (Dundee) described the effects of oral and intravenous administration of sulphopolyglucin in rats and humans. Oral absorption, as measured by lipaemia-clearing activity in the plasma and by measurement of SPG in the urine, was very poor, and the incidence of alimentary upsets following oral administration was high.

The meeting ended with a session on the haematological complications of the extracorporeal circulation, not reported here, at which the chairman was Professor D. M. DOUGLAS (Dundee), and the speakers were Dr. A. A. SHARP (Oxford), Mr. N. G. ROTHNIE (London), Dr. J. MATZKE (Copenhagen), and Dr. M. VERSTRAETE (Louvain).

NOMENCLATURE OF ABNORMAL HAEMOGLOBINS

During the Eighth International Congress of Haematology last month in Tokyo, 44 members met to discuss the nomenclature of the human haemoglobins. The absence of several distinguished investigators in this field was acutely felt. The following recommendations are therefore being sent to appropriate journals so that investigators not present will be able to criticize them in public.

Recommendations

1.—The recommendations on nomenclature made at the Symposium on Abnormal Haemoglobins in Istanbul, 1958, and published in 1959,[1] are endorsed and the letters A–N (with the exception of B), and S, are recognized as naming haemoglobins as there defined.

2.—The description of the variants of haemoglobin M as M_B, M_M, M_S (from Boston, Milwaukee, and Saskatoon respectively) is accepted,[2 3] and it is suggested that new haemoglobins M are described with fully subscripted names until they have been shown to differ from these three, when they should be given subscript initials (M_{Iwate}, possibly later M_1).

3.—The letters O, P, and Q are being allotted to the haemoglobins described under these letters.[4 5 6]

4.—Until the next meeting of the International Congress the letters R–Z (excepting S) should not be allotted to new abnormal haemoglobins, but these should be given names of localities. It should be left to the individual workers to choose the most meaningful name from the origin of the propositus, or the laboratory, hospital, town, or district where the haemoglobin was found. A new name should not be allotted in this way unless it has been ascertained that the haemoglobin to be named is different from all those adequately described in the literature.

5.—Of the two designations of the haemoglobin A_2 variant: A_2' and B_2,[7] the first is found more acceptable. If a third variant should be found it should be named A_2'' and not C_2.

6.—The names of the three known peptide chains of human haemoglobin are α, β, and γ,[8] and it is suggested that the normal chains should be designated in that way (i.e., not α^A or α^F, β^A and γ^F). The genetic superscript for the normal gene product + ($\alpha+$, $\beta+$, $\gamma+$) will not be used as it implies to the chemist a positive charge.

7.—The expressions β_A for H and γ_A for Bart's may be used when their identity is fully accepted. However, until the next meeting of the International Congress the traditional names should be mentioned at least once in each publication.

8.—The present custom to describe an abnormal chain by adding the name of the appropriate abnormal haemoglobin in superscript should be maintained ($S = \alpha_2\beta_2^S$: Hopkins-2 $= \alpha_2^{Hopkins\text{-}2}\beta_2$).

9.—A polypeptide chain should not be designated with a new small Greek letter (such as δ, ε, etc.) until chemical evidence for complete separate identity from the α, β, and γ chains (such as exists between these chains themselves) has been established, genetic differences notwithstanding.

10.—It is expected that the analysis of the amino-acid sequences in the globin molecule will eventually be followed by a precise chemical nomenclature. Meanwhile if a haemoglobin has been identified by the usual methods of electrophoresis, chromatography, spectroscopy, alkali denaturation, cold denaturation, and solubility tests, it should be described by the accepted capital letter as hitherto (S, C, D, G, E, etc.), as recommended by the Working Party meeting at the Sixth International Congress, Boston, 1956.[9] If comparison has been made on the same lines and with the same completeness with a haemoglobin carrying the names of a locality, that name should be applied. If the abnormal chain is identified this should be indicated by a subscript (for example, D_α, D_β); and until the full identity by examining the amino-acid sequences has been established this subscript should be followed by a declaration of origin ($D_{\beta\ Los\ Angeles}$, $G_{\alpha\ Ibadan}$). This implies that $D\gamma$ will have to be renamed $D_{\beta\ Punjab}$. If two or more of such haemoglobins are then found identical by analysis of the amino-acid sequences, only the name of the haemoglobin which was first discovered and fully defined by the conventional methods should be retained. For example, if $G_{\alpha\ Ibadan}$ and $G_{\alpha\ Azuakoli}$ are found to be identical regardless of which the amino-acid sequence has been fully examined first $G_{\alpha\ Ibadan}$ should be the remaining name. However, until the next meeting of the International Congress the alternative names should be mentioned at least once in each publication.

11.—No generally acceptable name was agreed upon for the familial condition in which haemoglobin F persists into adult age without morphological changes of the red cells and without anaemia. The term non-microcythaemic thalassaemia was considered not specific enough, as it might equally apply to the familial condition where haemoglobin A_2 is raised without associated morphological changes. If the expression "high F gene" is used this should be done with reservation and only provisionally until further knowledge allows better terminology.

12.—If several haemoglobins are present the phenotype should be designated by listing the haemoglobins in order of decreasing concentration regardless of genetical considerations (sickle-cell trait = AS, sickle-cell anaemia = SF, sickle-cell thalassaemia = SAF, or SFA, etc.).

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Christmas Gifts Fund

SIR,—Once again I ask your readers to give support to the Christmas Gifts Fund organized by the Royal Medical Benevolent Fund. Although we are able to give far larger regular grants than in the past, it is difficult for our subscribers to realize what extraordinary joy and happiness the Christmas gifts bring to our beneficiaries, to each of whom last year a gift of £8 was sent. To the old, the poor, and the lonely Christmas Day only too often brings poignant memories of happier days gone by, and the arrival of our gift gives great pleasure, as the letters of thanks testify so vividly.

The magnificent response to these annual appeals shows that they touch a special chord of sympathy. Because of this I appeal to you all to help bring Christmas cheer into the homes of many of our less fortunate brothers and sisters. Please send your contributions, marked "Christmas Gifts," to the Royal Medical Benevolent Fund, 37, St. George's Road, Wimbledon, London S.W.19.—I am, etc.,

R. M. HANDFIELD-JONES,
Chairman, Committee of Management,
Royal Medical Benevolent Fund.

Oral Diuretics in Pregnancy Toxaemia

SIR,—We would like to be allowed to reply to some of the correspondence sent to you (and privately to us), as a result of our original letter (June 11, p. 1807). Knowing how widespread the use of diuretics for toxaemia was, we confess we were pleasantly surprised by the agreement with our sentiments expressed by all the writers of the first two or three batches of letters. Yet some of what we wrote has been a little misunderstood; for we never stated that diuretics killed a foetus *in utero* . . . merely that in spite of diuretics babies died *in utero*, possibly because the progress of the toxaemia was less easily followed, and strict supervision slackened, so that indications for early induction were missed.

We were not surprised to see letters claiming that large series of cases had been treated successfully; such a series was published in March, 1960, in the *Journal of the Irish Medical Association*; and we knew of others. In a common condition like this unless a large series of cases is taken and carefully reviewed, with all the details of cases under review fairly presented, and assessed statistically, numerical impressions are of no value. We therefore would not wish to be drawn into giving any statistics as to the total number of cases we have treated, and in what total number of cases treated these five deaths occurred. Nor did we wish to become involved in drawing up a lengthy medical memorandum on the clinical details of these five cases. We merely say that they occurred both in primigravid women and multiparous women. We would not like to define even whether the toxaemia was severe or otherwise, because, as is clear in your correspondence columns of one day only, September 10 (p. 800), we see the futility of attempting such descriptions. Dr. Rezsö Nagyivanyi, of Budapest, in his careful and thoughtful letter, claims that he has treated more than 100 cases without intrauterine death or noxious effects to mother or foetus. A hundred per cent. success rate is indeed an enviable figure to achieve. Dr. Richard Sands, on the other hand, states that it is "common knowledge that in the past foetal and infant loss in severe pre-eclampsia approached 20%, and this was long before chlorothiazide diuretics were used." We do not know what criteria he uses to call a case severe. With or without diuretics our mortality rate is usually much lower than 20%; but it varies according to the care received by the patient and other circumstances.

We decided to try the oral diuretics early on. Unfortunately we did not from the beginning conduct a firm statistical research into their action; partly because we accepted reports of their efficacy, and partly because we are conducting, in our department, other research into toxaemia of pregnancy. We have a yearly turnover of some 350 in-patients with toxaemia in the department. We think that diuretics may be *indirectly* responsible for foetal death, by masking signs of the toxaemic process. Nothing any of your correspondents has produced suggests otherwise. We were particularly impressed by Dr. Nagyivanyi's reasoning that oral diuretics do nothing in the way of causative treatment, but may be very valuable to offset the oedema suffered by toxaemic patients and to improve their general condition before labour, *provided* the patients are under careful observation, in hospital, and provided careful watch is kept on the electrolyte equilibrium. We would also add provided every early sign of foetal embarrassment is carefully looked for and appropriate action taken, which in the majority of cases will mean a timely induction of labour.

One of us still uses diuretics with these precautions, and it may be that with these very careful details of supervision diuretics have their place. There is, however, no evidence that such careful and extra supervision is *generally* carried out. On the contrary, we wrote our letter because it was our experience, and we were disappointed to find it happening even in our own department, that as the valuable sign of oedema was lost, so the supervision of the patient became less instead of more strict.

If we have only managed to point the lesson that stricter supervision is required when oral diuretics are used, our letter will have served some useful purpose. We had hoped that one or other of your correspondents would have indicated to us something about the method of action of oral diuretics on the toxaemic process, but this has not been forthcoming. Therefore, the problem still remains to be investigated, as we have said in our original letter. Until a paper is produced showing the results of this investigation diuretics should probably be used in toxaemia of pregnancy only in units with research facilities. This is our contention.—We are, etc.,

Oldchurch Hospital, Romford.

JOHN D. WATT.
ELLIOT E. PHILIPP.

Vacuum Extractor in Obstetrics

SIR,—We have delayed commenting upon the letter of Mr. E. W. Lillie (August 20, p. 602) in the hope that the points he discussed might be further elaborated in correspondence from other users of the instrument. Our experience of the use of the vacuum extractor in the very early first stage of labour is limited to two cases in which the cervix was only two fingers dilated and not completely effaced. The first of these was case 87 described in our paper (June 4, p. 1684). In the second, a recent case, delivery was undertaken at two-fingers dilatation on account of prolapse of the cord, and the cervix was torn in our efforts to achieve prompt extraction of the foetus. In both these cases we feel that the trauma to the cervix was such that this particular application of the instrument should be avoided. Further, the risk of scalp necrosis associated with prolonged traction which has been described by

Malmström,[1] and which led Antoine[2] to abandon the use of the instrument, has been another factor which has restricted our use of the instrument early in the first stage. Lillie himself at the Royal Society of Medicine described "trauma to the obstetrician" resulting from the fact that delivery took at least an hour in each case. We await with great interest, however, details of his further experience in this special field which he describes.

We cannot agree with the comments expressed in the last paragraph of his letter, that "any obstetrician who is reasonably skilled in the use of forceps will find few indications for the vacuum extractor in the second stage of labour." We have already stated the advantages which in our opinion are to be derived from the use of the instrument in the late first stage of labour. In the second stage also, we feel that in very many instances the vacuum extractor is preferable to the forceps for the following reasons: (1) The absence of encroachment by the instrument on the birth canal. (2) The lessened necessity for anaesthesia. (3) The reduced trauma to mother and foetus. (4) The improved management of malpositions of the head and of certain malpresentations.[3] (5) Increased simplicity of technique. These we have discussed in detail elsewhere, and it would serve no useful purpose to go further into the matter here, but we must reiterate that in our experience the "ventouse" can offer many advantages over forceps, not only in complications of the first stage of labour but also in the second stage. We have not regarded it as a means of accelerating normal labour, but rather as a valuable aid in our management of a considerable range of problems of abnormal labour. Further, we feel that Mr. Lillie's advocacy of a restriction of the vacuum extractor to the first stage of labour would tend to hinder its use in the problems of domiciliary practice. In this field we believe that many of the great potentialities of the instrument which he mentions may lie.—We are, etc.,

J. A. Chalmers.
R. J. Fothergill.

Ronkswood Hospital, Worcester.

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[1] Malmström, T., *Acta obstet. gynec. scand.*, 1954, **33**, Suppl. 4
[2] Antoine, T., personal communication, 1959.
[3] Chalmers, J. A., *Proc. roy. Soc. Med.*, in press.

"Obstetric Helper"

Sir,—So far as we can ascertain, there is no type of "obstetric helper" (that is, lithotomy support for domiciliary use) which has not the disadvantages of applying excessive pressure either to the back of the neck or to the acutely flexed popliteal fossae, or to both, and of tending to cause flexion of the lumbar spine.

One of us (P. R. B.), after twenty years of seeing patients suffer from these discomforts, has tried to devise an improved pattern. The result, shown in the illustrations, consists of a central adjustable waist-strap from each end of which an adjustable leg-strap passes in front of the knee of its side to a stirrup supporting the foot. We claim that it is possible for a conscious patient to rest fully relaxed while the legs are so supported, and, contrary to what one might expect, there is no tendency for the leg-strap, resting on the depression between the patella and the internal condyle, to slip off the knee. The natural curve of the spine in the lumbar region is maintained by the pull of the leg-straps on the waist.

We have now been using this support for over a year for suturing perineal tears under local analgesia, and

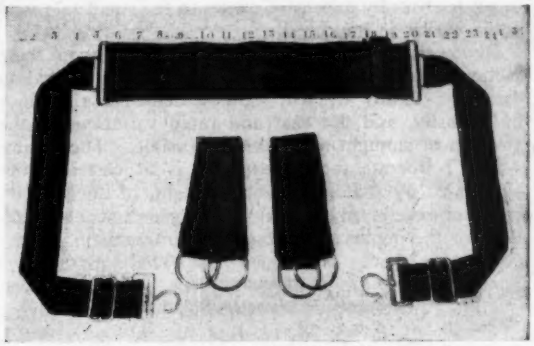

Fig. 1.—The parts of the "obstetric helper."

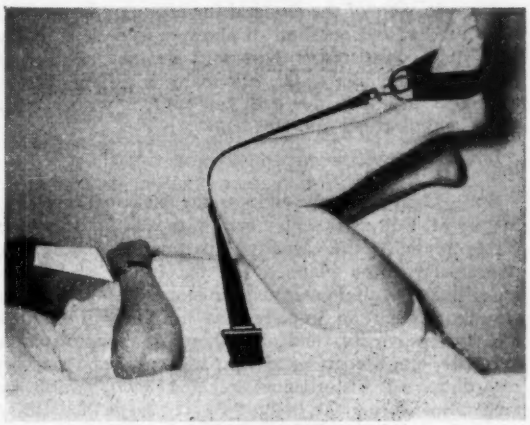

Fig. 2.—"Obstetric helper" in use.

patients (particularly those who had already experienced the lithotomy position either at home or in hospital) have expressed satisfaction.

Dr. Edith Bruce Wilson kindly allowed one of us (M. J. T.) to try out the support in her practice in Wood Green. Messrs. A. L. Hawkins & Co., 15 New Cavendish street, W.1, are the makers.

—We are, etc.,

P. R. Boucher.
Margaret J. Turpin.

Winfrith, Dorset.
London N.22.

Theatre Lighting

Sir,—In considering the enormously expensive and complicated lighting for operating theatres (page 10 of the pictorial supplement on hospital design in your issue of September 10), I am struck by one fallacy in it—it does not allow for the thickness of the human skull. No amount of illumination of the surgeon's occiput will enable him to see into a narrow crevice, and there are few operations in which the necessity for this does not exist from the start, or might not arise later. The simple test of trying to see clearly the whole interior of an ordinary fountain-pen cap will illustrate this; it can only be done by a light which starts in front of the cranial obstruction; that is to say, a headlight. (I omit the distal illumination needed for long narrow tubes such as urethroscopes in which no questions of parallax arise.) I suggest that there is a great need at present for a really efficient general-purpose surgical headlight: I have designed one myself[1] which is fairly satisfactory,

but it is absurdly expensive owing to the small sale, and could easily be improved.

However, one important principle emerges from these pictures—that daylight has no place in an operating theatre. Really efficient lighting demands a balance of intensity, and the vast and rapid variations in the strength of sunlight make this impossible. The theatre where I operate most frequently is at certain times penetrated by shafts of direct sunlight, of an intensity which completely throws out the surgeon's accommodation for the depths of a wound.—I am, etc.,

London W.1. DENIS BROWNE.

REFERENCE

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Our Hospitals

SIR,—In view of the demand for economy in hospital building, has the question of showers as well as baths been duly considered? Not only are they cheaper to install and use less water, but many a patient who is incapable of sitting in a bath can enjoy a proper wash under a shower.—I am, etc.,

Tavistock, Devon. T. M. DAVIE.

SIR,—May I heartily endorse the plea made by Dr. Muriel M. Edwards (September 24, p. 938) for reception wards adjoining the casualty departments of hospitals, particularly those planned for the future? I have, unfortunately, on numerous occasions during the past few years been an in-patient at hospitals in London and the provinces, and can therefore support from personal knowledge and experience her remarks regarding the disturbances created in a ward by admissions during the night.

I feel sure that well-organized reception wards which could cater for all types of emergencies, say between the hours of 8 p.m. and 8 a.m., would not only be a boon to the night staff of all other wards and their patients but also to those doctors and members of ancillary services on call, who certainly would know exactly where to make for, thereby avoiding much frustration and energy at times when one is bound to feel tired. Maybe there are administrative difficulties, but these should be studied well and considered at length so as not to overrule something of great importance which by her letter has once more been brought to note—namely, one method of counteracting noise and disturbance in hospital wards at night.—I am, etc.,

Pyle, Glam. R. J. PHILLIPS.

Megimated Barbiturates

SIR,—With regard to the memorandum by Drs. B. W. McGuinness and F. J. Roberts (October 1, p. 996) relating to megimated barbiturates, I would like to report the following case.

The patient, a physically healthy woman of 25 years, was admitted at 10 p.m. with a history of taking 94 "mylomide" (amylobarbitone 100 mg., bemegride 10 mg.) tablets at noon of the same day. On admission the patient was almost comatose. She responded to painful stimuli, the pupils responded to light, all tendon jerks were diminished, and the plantar responses were flexor. All limbs moved. The pulse rate was 84/min. and the blood-pressure was 100/60. "Methedrine" (methylamphetamine hydrochloride), 30 mg., was given by slow intravenous injection, and the level of consciousness improved. At 11 p.m. the nurse reported that the patient was in coma which had been preceded by a twitching of the facial muscles and a frothing at the mouth. On examination the patient responded to no stimuli for several minutes and the limbs remained flaccid. I surmise that she had suffered a modified epileptiform seizure. She remained drowsy for 24 hours, but had completely recovered by 48 hours.

—I am, etc.,

Southern General Hospital, Glasgow S.W.1. C. P. HELLON.

Addiction to Hypnotics

SIR,—Dr. Allen A. Bartholomew (July 30, p. 388) casts his net too wide in implying that personality factors concerned in certain types of addiction would apply to all who regularly smoke, drink, or take drugs. As inferred in the Noyes's typology he quotes, the problems of addiction are clearly multifactorial and related to individual differences (some individuals become rapidly addicted to a drug—others do not) as well as to specific instances (some drugs often lead to addiction—others rarely). The question of the recognition of individual differences before addictive behaviour occurs is altogether different but resembles so many other problems in psychiatry to-day.

Of patients admitted to hospital because they have been consuming alcohol to excess a few will be clearly schizophrenic; some will be described as neurotic; others as psychopathic or simply alcoholic. In a group of women who had been taking carbromal to excess the personality profile which emerged was remarkably constant and might be described as extraverted neurotic. Most had exhibited neurotic symptoms before they started drug-taking, and in the light of many recurring features (in terms of interpersonal relationships, pill-taking habits, etc., before addiction) the concept of dependence seems clinically appropriate in certain patterns of drug habituation or addiction, although Dr. Bartholomew's inference that all cases of addiction have a common causation is untenable. At all events, the fact that this type of patient rapidly finds an alternative when supplies of one drug are unobtainable suggests that the particular pharmacological agent is not always of sole importance.

Atkinson[1] has since published a study of a similar group of patients and concludes that the "patients affected are those liable to habituation with any drug supplying a psychological need," whilst others describe the "habituation-prone"[2] or "predisposed personalities."[3]—I am, etc.,

Heathcote, Perth, Western Australia. I. PIERCE JAMES.

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[2] Glatt, M. M., *Lancet*, 1959, 1, 887.
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Side-effects of Phenelzine

SIR,—I was interested to read the letter by Drs. J. Johnson and M. D. Eilenberg (September 17, p. 857) describing three cases of mania produced by this drug. This illustrates the truism that endogenous depression is not an entity in itself but is only one aspect of the manic-depressive syndrome. Thus any treatment for depression, whether it be E.C.T. or even amphetamine, can turn the clinical picture into that of mania, especially if the dosage or number of treatments is in excess of standard practice. From the histories given it is evident that two of these patients were given a greater amount

of phenelzine than is commonly prescribed, and one of them had treatment for rather a long period.

In hospital practice it is easy to control treatment, since slight changes of mood are detected quickly and manic reactions are not seen so frequently now as they were formerly. Out-patient psychiatry has a great many advantages, but it is important to recognize that risks are run, although in the main the benefits of out-patient treatment appear to outweigh its occasional disadvantages.—I am, etc.,

Cane Hill Hospital, Coulsdon, Surrey. JOHN T. HUTCHINSON.

Haemopericardium during Anticoagulant Therapy

SIR,—I wish to report a curious cardiac case:

On April 3, 1960, a young man of 27 years was admitted to Farnham Hospital with the history of a sudden, severe, tightening pain across the front of the chest at about 6 p.m. the previous day while at work. He was breathless and nauseated, sweating profusely. The pain was constant and kept him awake all night. On admission he looked very ill and shocked. His temperature was 102° F. (38.9° C.), pulse 120 and regular, B.P. 110/70; heart sounds were pure and the lungs clear. An E.C.G. showed marked S.T. segment elevation; serum transaminase (S.G.O.T.) was, however, only 12 Cabaud units and remained so in consecutive tests. His E.S.R. was 75 mm. after 1 hour (Westergren), Hb 86%, serum cholesterol 145 mg./100 ml., W.B.C.s 21,000 with 65% polymorphs. A portable chest radiograph showed no abnormality. Blood culture was sterile and the sputum contained no acid-fast bacilli. It was decided to treat him as a case of coronary thrombosis. After an initial course of heparin and phenindione (" dindevan ") together, his prothrombin concentration was maintained at 10 to 15% (Quick) on phenindione alone 75 mg. once daily.

On May 3 a pericardial rub was heard, and this continued loud for the next seven days, and then became indistinct; the heart sounds were also distant. At the same time the patient was deteriorating, his temperature remained at 102° F. (38.9° C.) and Hb fell to 50%. A pericardial effusion was confirmed by chest radiograph. On May 12 a needle was inserted into the pericardium and one pint (0.6 l.) of blood aspirated. He was given vitamin K immediately; he had no more phenindione. The effect was dramatic. The next day his temperature was down to normal, and he felt progressively better. A week later his Hb was 75%, the cardiac outline being within normal limits. On June 2 he was discharged home.

This was an extraordinary case. When the patient was admitted his symptoms suggested a large myocardial infarct. However, his youth, persistently low transaminase, and rather protracted pyrexia appeared to be strong evidence against it. The pericardial rub fitted in with cardiac infarct. In pericarditis *per se* a friction rub is heard early, even only transiently. On the whole it is considered probable that he had a myocardial infarct and the haemopericardium might be due to the anticoagulants.

I would like to thank Dr. J. W. Todd for his help and permission to report this case.

—I am, etc.,

Farnham Hospital, Farnham, Surrey EZEKA E. OKAFOR.

" Persantin " in Coronary Disease

SIR,—Although Drs. Tom Foulds and John Mackinnon (September 17, p. 835) report that oral " persantin " has no place in the treatment of angina, I have been using the drug intravenously for the treatment of the severe pain associated with coronary thrombosis, and have found that frequently 10 mg. intravenously relieves the pain in less than five minutes.

—I am, etc.,

Chase Farm Hospital, Enfield, Middx. T. SIMPSON.

Insulin-independent Young Diabetics in Natal

SIR,—The description by Dr. G. D. Campbell of " insulin-independent young diabetics in Natal " (August 13, p. 537) largely echoes my own findings in a previous series of patients.[1] These patients were then described as " . . . a further distinct group of young diabetics, between the ages of 20 and 40 years, who require less than 75 units daily, but these cannot be regarded as belonging to type 1. They were all free of ketosis, and most of them were overweight women. But for their earlier age of onset, they resemble type 2 diabetics." Approximately 15% of patients in the series belonged to this group. When this survey was made (1956–7) oral hypoglycaemic agents were not widely used, so their effect on this group was not determined. The lower insulin requirement, compared with the dose of about 100 units daily quoted by Campbell, may be accounted for by the fact that all the earlier patients were controlled in hospital and subjected to stricter dietary control than is possible in out-patients.

My own results with oral treatment of these Indian diabetics have been less encouraging than those quoted by Campbell.[2] We have tried various oral hypoglycaemic agents (mainly chlorpropamide) on 55 Indian diabetic in-patients at this hospital. Using urine tests and random blood-sugar estimations as criteria of control, we have found that the oral therapy has substantially affected the diabetic state in less than one-fifth of the patients. Many of the remainder have been maintained on the treatment, but with poor control and largely as a measure of desperation in circumstances where diet is impossible and insulin potentially dangerous to out-patients. It must be admitted that many of these diabetics would, by European or American standards, not be considered ideally selected for oral therapy. Many of them are young diabetics with insulin requirements above 40 units per day. Our conclusion is that none of the drugs used so far (tolbutamide, chlorpropamide, and biguanide) can be regarded as a panacea for diabetes among the Indians. Experience with these drugs among a larger series of African diabetics has been no better.

That insulin is potentially dangerous has been shown by several instances of severe hypoglycaemia in young Indians of " J " and " insulin-independent " types who had been controlled on insulin because of complications or lack of response to oral treatment. In this respect our experience differs from that of Campbell, who records that hypoglycaemia never occurred in his diabetics of these types. Ketosis is admittedly rare but still appears, and may be severe, in these diabetics when they are complicated by infections. For this reason the term " insulin-independent " may be misleading. No diabetic is yet independent of insulin when he is ketotic or the victim of other severe complications.

These variations in experience in separate clinics are probably due to differences in technique and methods of observation. Degree of control of diabetics is difficult to standardize when there are so many variables. Similarly, the clinician who uses more insulin will see more cases of hypoglycaemia. Those who deal mainly with in-patients will see more ketosis and complications than their colleagues whose duties lie mainly in the out-patient department. The important fact which has

emerged from studies of diabetes in tropical and subtropical countries is that there is a group of young, insulin-resistant diabetics, fat and thin, of Indian and African extraction, who do not normally require insulin to keep them free of ketosis.—I am, etc.,

Edendale Hospital, Pietermaritzburg, South Africa. J. E. Cosnett.

References

1 Cosnett, J. E., *Brit. med. J.*, 1959, **1**, 187.
2 Campbell, G. D., *Med. Proc.*, 1959, **5**, 559.

Gangrene of the Scalp

Sir,—A case similar to that reported by Drs. P. Fleischl and B. E. Oldham (August 6, p. 439) is described here and is another example of scalp gangrene associated with cranial arteritis.

A diabetic man, aged 75, gave a three months' history of headaches typical of cranial arteritis. In a period of three weeks areas of discoloration in both temple areas became blistered and then developed into dry, hard, dark, necrotic patches (see photograph). Two weeks previously he totally lost the vision in the left eye. He felt generally unwell, complained of multiple joint pains, and had lost one stone (6.4 kg.) in weight.

Examination showed that he was febrile. The temporal pulse was absent on the left side and diminished on the right. The left optic fundus showed the appearance of central retinal artery occlusion, but there were no diabetic eye complications. Haemoglobin was 66% (9.6 g.), white count 6,100, E.S.R. 65 mm. (Wintrobe). The diabetic state was well stabilized. He was immediately admitted to hospital and treated with prednisolone acetate by the intramuscular route, as he was known to have a duodenal ulcer. The starting dose was 40 mg. three times a week, which was later reduced to 30 mg. three times a week. Salicylate analgesics were avoided. There was rapid improvement. Pain and malaise disappeared, the fever settled, and the E.S.R. steadily dropped to normal. The necrotic patches did not alter in appearance and left-sided optic atrophy became obvious. After six weeks' treatment he developed dyspepsia for two days, followed by a melaena, from which he made a good recovery, only to die three weeks later from an anterior cardiac infarct. Necropsy confirmed the presence of a duodenal ulcer and coronary atheroma with thrombosis. The affected cranial arteries were not examined.

—I am, etc.,

Royal Victoria Hospital, Bournemouth. Justin Clark.

Folic-acid Absorption Tests

Sir,—May I comment on Dr. J. Badenoch's statement in his first Goulstonian lecture on "Steatorrhoea in the Adult" (September 24, p. 879) that "folic acid is absorbed mainly from the jejunum," and that tests of folic-acid absorption therefore serve as tests of function of the upper gut? This view, which was quoted in a recent symposium at the Royal Society of Medicine,[1] is based on the observation[2] that patients with regional enteritis involving the ileum excreted normal amounts of folic acid in the urine after 5 mg. by mouth. By contrast, the excretion was abnormally low when there was apparently isolated jejunal involvement in this disease. This method of studying folic-acid absorption by its excretion in the urine was elaborated by Girdwood.[3]

The results of a folic-acid absorption test which employs the change in the serum level of folic acid as an index of absorption,[4] in 14 patients with regional enteritis, are shown below. These patients had varying degrees of involvement of the ileum. The test was abnormal in all but one of these cases.

	Peak Serum Folic-acid Level after 40 μg./kg. Orally		
	0–30 (μmg./ml.)	31–50 (μmg./ml.)	51–140 (μmg./ml.)
Normals (68)	0	0	68
Regional enteritis (14)	7	6	1

The explanation of the normal urinary excretion of folic acid in these patients probably lies in the lesser sensitivity of this method as compared with the tolerance-type test. Patients with malabsorption syndrome who show peak serum folic-acid levels between 25 and 40 μmg./ml. after 2 to 3 mg. by mouth usually excrete normal amounts of folic acid in the urine when given 5 mg. of the vitamin. The peak serum folic-acid levels were within the normal range (55 and 72 μmg./ml. in two tests) in a patient who had 8 ft. (2.4 m.) of proximal gut resected for jejunal diverticuli.[5] Possibly patients with jejunitis and malabsorption of folic acid have far more extensive involvement of small gut than is apparent.

Under physiological conditions dietary folic acid, which is usually less than 0.2 mg. daily, may well be absorbed from the jejunum. However, under test conditions which employ relatively large doses of folic acid (2–5 mg.) it is probable that both jejunum and ileum are concerned, and disease of any part of the small gut, if sufficiently extensive, will impair the absorption of the vitamin. In the case of folic acid this impairment can be demonstrated at an earlier stage by a tolerance-type test than it can be with the urinary excretion method. Folic-acid absorption tests by either method are excellent tests of small intestinal function, but are certainly not tests of jejunal function alone.—I am, etc.,

London W.2. I. Chanarin.

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2 Cox, E. V., Meynell, M. J., Cooke, W. T., and Gaddie, R., *Gastroenterology*, 1958, **35**, 390.
3 Girdwood, R. H., *Quart. J. Med.*, 1956, **25**, 87.
4 Chanarin, I., Anderson, B. B., and Mollin, D. L., *Brit. J. Haemat.*, 1958, **4**, 156.
5 —— and Mollin, D. L., 1960. Unpublished observations.

Tight Nylons and Rubber Bands

SIR,—Recently I have seen two examples of mechanical constriction producing massive oedema. One in a middle-aged woman of average height, who presented herself with extreme oedema of the legs. As she was of good health and clinical examination revealed nothing abnormal, I was at a loss to explain the condition until I found that the upper end of her nylon stocking on each leg was pulled up very tightly and attached to one anteriorly placed suspender. This was causing the inner side of the stocking to cut deeply into the rather excessive subcutaneous fat of the thigh. She was instructed to wear stockings with a wider, turned-over top and to apply a suspender back and front. On inquiry later, I was informed that the oedema had completely subsided.

The other case was that of an elderly woman to whom I was called one evening to find the ring finger of the left hand intensely cyanosed and swollen. She was wearing a wide wedding ring which could not be slipped over the knuckle. Again there was no apparent cause. The ring was cut through and underneath was found an elastic band wound two or three times round the base of the finger. It was nearly buried in the oedematous tissues. Her son has now removed any elastic bands which she is likely to find, as she was in the habit of winding them round her fingers to avoid losing them.
—I am, etc.,

Wollaston, Northants. MARGARET B. CARTER.

Post-operative Obstruction Caused by a Swallowed Hair-grip

SIR,—A nulliparous woman, aged 52, was admitted on January 31, 1960, for hysterectomy. Physical examination showed her to be healthy apart from an enlarged uterus. Poliomyelitis as a child had left her with a wasted and short left leg.

On February 3, 1960, she had a total hysterectomy and bilateral salpingo-oophorectomy, when an enlarged fibroid uterus was removed. Post-operatively she vomited small amounts intermittently until the 6th day, when she brought up two pints (1.1 litres) of bile-stained fluid in 12 hours. She had had a good bowel action the previous day, and complained of mild abdominal discomfort, but no severe pain.

On examination her temperature was normal and pulse 100. Her abdomen was moderately distended and tympanitic; bowel sounds were scanty. The differential diagnosis lay between a paralytic ileus and an organic obstruction, possibly due to a loop of bowel being stuck to a raw surface or herniating between the peritoneal sutures. Blood count that day showed her haemoglobin to be 98%, and a polymorph leucocytosis of 14,000 cells/c.mm. Her blood urea was 107 mg.%, and she was salt-depleted and hyperkalaemic. She had two straight *x*-rays of her abdomen taken. The erect film showed the whole bowel to be distended, with some fluid levels. The other film, taken lying down, presented a similar picture, but it showed a hair-grip in the lower part of the descending colon: this was at first taken to be an artifact, as it was not visible on the other film (presumably since it dropped in the erect position).

She was put on to gastric suction and intravenous infusions, and the following day her serum electrolytes had returned to normal and her blood urea had fallen to 86 mg.%. Her abdomen, however, was still very distended, although she was passing a little wind and faecal fluid. At 11 p.m. that night she passed a little more fluid per rectum and the "kirbigrip" type of hairclip was found in the bed-pan. Thereafter her condition rapidly improved and she was discharged home on February 16, 1960. She was seen for follow-up examination two months post-operatively, when all her symptoms had subsided and she was found to have a satisfactory result.

This was a puzzling case, as the operation had been quite straightforward; obstruction on the sixth post-operative day suggested an organic cause, but the *x*-ray picture was more like that of an ileus, which we would have expected to present earlier. The latter, however, was unlikely in view of the fact that she had a good result from an enema, and two normal bowel actions. The finding of the hair-grip therefore solved our dilemma. The patient, when questioned, admitted that she was in the habit of putting these hair-grips in her mouth when she did her hair, but could not remember swallowing one. When this particular grip entered her gastro-intestinal tract we shall never know. The raised white-cell count suggested that it might have caused a little pericolic inflammation if not a frank perforation.

This case is reported to show that it is possible to swallow these hair-grips inadvertently, and also to present an unusual cause of post-operative obstruction.

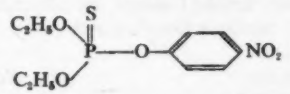
I am very grateful to Mr. P. R. Mitchell for allowing me to report this case, and for his encouragement throughout.
—I am, etc.,

Royal Hampshire County Hospital, Winchester. G. C. BRILL.

Parathion Poisoning

SIR,—I feel it worth while publishing five cases of parathion poisoning, one of them with at least 39 ileo-ileal intussuceptions.

Parathion is an organic phosphorus compound with the chemical name, O,O-diethyl-O-*p*-nitrophenyl thiophosphate, and the chemical formula:



It was first prepared in German laboratories and was known as E605. It is widely used as an insecticide in agriculture. It acts as a very highly active, irreversible inhibitor of the enzyme cholinesterase, and thus allows the flooding of the body with huge amounts of acetylcholine, with the usual cholinergic signs and symptoms. These include headache, giddiness, blurred vision, weakness, cramps, diarrhoea with loss of sphincteric control, discomfort in the chest, sweating, miosis, tears, salivation, pulmonary oedema, cyanosis, uncontrollable muscle twitches, especially in the face and pectoral regions, coma, and death. Miosis, severe pulmonary oedema with bubbling chest and froth at the mouth and nostrils, and the uncontrollable muscle twitches are very characteristic. Following the ingestion of parathion, death has been essentially instantaneous.

A boy of 17 years who ingested about 15 ml. of the poison fell dead practically instantaneously; another boy of 19 years became unconscious in 10 minutes and died 25 minutes after the ingestion of a small amount of the poison. A third case, a girl of 15 years who put a few drops of the poison in her mouth, but spat them out immediately, became unconscious in 20 minutes and died 25 minutes later. Another boy of 13 years, who ate fruit recently sprayed with the solution of parathion, showed toxic symptoms in two hours and became unconscious three hours later; with treatment, he recovered consciousness and became orientated and enjoyed a meal, only to lapse into coma again and die about 20 hours after ingestion of the poison.

Parathion poisoning can occur through dermal contact, too, but symptoms may be delayed up to eight hours after exposure: a child of 25 months, the fifth case, who spilled a small amount of the poison over his garments, started to show toxic symptoms after eight hours, became unconscious, and died 16 hours after exposure.

Absorption of parathion through the respiratory tract can occur, but probably only to a slight extent, because the vapour pressure of parathion is so low that respiratory exposure alone is usually not sufficient to cause serious poisoning. I have never come across any case of poisoning of this sort. Most cases of poisoning in persons working in spraying the poison have some dermal exposure at the same time.

Pathology.—All post-mortem findings, whether gross or microscopic, are insignificant except for those associated with pulmonary oedema, cyanosis, and those secondary to convulsions. A constant pathological finding which probably has not been recorded before is the congestion of the terminal few feet of the ileum. This was found in all cases of parathion poisoning I examined after death. Congestion was diffuse, involving the whole circumference of the ileum, except in one case where the congestion was patchy, mainly on the anterior wall and the antimesenteric border. This appearance did not differ whether the post-mortem examination was done shortly after death or when it was delayed till next day.

In one case only of my series, the child of 25 months who died of parathion poisoning through dermal exposure, I found at least 39 ileo-ileal intussusceptions. The length of each intussusception varied from three to ten centimetres; none of them showed obstructive symptoms, and all reduced very easily. I have never heard of this happening before; probably it was due to the incoordination and excessive peristalsis of the small intestine.

Parathion, an organic phosphorus insecticide, is a cheap deadly poison. To the usual cholinergic manifestations of parathion poisoning, two pathological findings may be added—namely, the occurrence of congestion in the terminal ileum in all cases, and the occurrence of multiple ileo-ileal intussusceptions in one case.—I am, etc.,

Amman, Jordan. E. Handal.

Preventive Medicine

Sir,—Professor E. M. Backett's letter in *The Times* of September 12, entitled "Family Doctor of the Future: New Problems He Must Face," has raised an important and urgent question. As a general practitioner for 60 years, now retired, and medical examiner for four life insurance companies, this problem of the early diagnosis and treatment of chronic disease has long occupied my thoughts. Many years ago I wrote to the life insurance companies suggesting a yearly examination of all insured persons, in order to diagnose and treat any signs of early disease. This suggestion was rejected on account of its impracticability, but now when the whole population is registered under the N.H.S. it would be quite possible for the Minister to advise a yearly examination as a normal precaution. Dr. John Hunt from his experience while visiting Russia draws one particular conclusion from his visit—namely, that preventive medicine is one of the main objects of Russia. Many times in the past I have been able to advise friends or patients to consult a doctor owing to the fact that I have observed early signs or symptoms of disease overlooked or ignored by themselves. As a young medical student over 60 years ago I was able to assist my father, then chief medical officer to the Privy Council, in preparing articles on preventive medicine, and ever since I have been impressed by its immense importance, both from the point of view of prevention and also from that of saving the nation literally vast sums of money.—I am, etc.,

Weybridge. R. Thorne Thorne.

Lumps in the Breast

Sir,—I would like to endorse every word of Mr. Brian McN. Truscott and Dr. D. G. Brotherton's letter on lumps in the breast (September 17, p. 857). I have always been of the opinion that every lump in the breast should be excised for biopsy. Obviously most of these lumps will be benign, but some may well become malignant at some later stage.

We are exhorted by Mr. D. F. Ellison Nash (October 1, p. 1018) to regard lumps in the breast with masterly inactivity and to treat the patient. Treat the patient for what? Surely to wait for confirmatory evidence such as axillary adenitis is to shut the stable door after the horse has bolted. It seems unlikely that many infected cysts would be removed—and general anaesthesia would minimize any risk—and advanced neoplasms would not arise if the original lump had been excised in the first place. If and when my wife has a lump in her breast I shall make it my business to have it removed for biopsy without delay.—I am, etc.,

Osgathorpe, Nr. Loughborough, Leics. W. M. L. Horner.

Sir,—I submit that the only safe way to treat these is to cut down and have a look. If innocent it can be shelled out, and if malignant radical measures adopted without loss of time. I would like to quote a case in support.

Some years ago an Army teacher in Malta discovered a breast lump and reported to her M.O., who assured her it was harmless. Later, she was seen by the surgical specialist, who agreed. A year or so later she was transferred to Aldershot and saw an R.A.M.C. surgeon, who also reassured her. However, the lady was worried, and one day, being on a visit to Croydon to her sister, she was persuaded to let me examine her.

After a most careful examination I could only agree with her previous advisers. But as she was very worried I arranged for her to have one more examination, and by one of the foremost surgeons in London, who reported, "The lump is a cyst, and to convince the lady I put in a needle and withdrew some fluid." He also arranged to admit her to a nursing-home to have the cyst excised, and invited me to be present and assist. At the operation, the cyst was there all right, but beneath it was a carcinoma. The surgeon thereupon did a radical mastectomy under difficulties, as he had not expected or prepared for an extensive operation.

The after-history was tragic. Within six months secondaries were manifest, and in eighteen months the patient died.—I am, etc.,

Ipswich, Suffolk. Charles Mills.

Efficacy of Psycho-analysis

Sir,—In your issue of August 27 (p. 671) I stated that Dr. H. L. Freeman and Mr. D. C. Kendrick had been guilty of gross inaccuracy when, apparently quoting from my book on *The Technique of Psycho-analysis*,[1] they maintained (August 13, p. 497) that I "disavowed" any claims to the therapeutic usefulness of psycho-analysis. On September 17 (p. 863) Mr. Kendrick produced two quotations which he "interpreted as

meaning that Dr. Glover has no confidence in the therapeutic efficacy of psycho-analysis," adding, however, "this may be a misinterpretation." My present object is simply to point out that it is indeed a misinterpretation, one that could have been avoided by a more careful study of the context of the quotations. The article in question was in fact an analysis of the therapeutic criteria of psycho-analysis in course of which I listed a number of unwarranted assumptions that tended to cloud the issue. Amongst these I included all glib assumptions regarding the wholesale applicability of psycho-analysis, which in my view gave rise to "criteria which are at the same time perfectionist, undefined, and uncontrolled." For this reason and because, in my opinion, the methods of statistical control of results are quite inadequate, I excluded the factor of therapeutic efficiency from a list of twenty-four criteria which I proceeded to discuss.

May I take this opportunity of quoting two other passages from this article? First, regarding unchecked impressions, "If to the welter of clinical variables we add a number of methodological variables we cannot attach *any* scientific significance to general impressions or assumptions regarding *any* form of psychotherapy"; second, apropos the desirability of research on the subject, "Psycho-analysis has no need to keep up appearances, but it does need to delimit as accurately as possible its uses as a therapeutic agent." For the rest I would merely repeat that the book in question was concerned with the efficacy of psycho-analytic technique in "accessible" and "moderately accessible" cases and its uses in "intractable" cases, a fact which seems to have escaped the attention of both Mr. Kendrick and Dr. Freeman.—I am, etc.,

London W.1. EDWARD GLOVER.

REFERENCE

[1] Glover, E., *The Technique of Psycho-analysis*, 1955. Baillière, Tindall, and Cox, London.

Child Psychiatry

SIR,—The letters of Dr. Bridget K. Attlee and Dr. Freda Reed (September 3, pp. 737 and 738) and Dr. Barbara K. Howells (September 17, p. 862) have raised the issue as to whether lady doctors with families (and possibly others) might have in-service training at child guidance clinics and so become competent clinical assistant child psychiatrists at these clinics.

The suggestion seems to me to be, on principle, a good one, and doctors whose personalities are suitable should be able from such part-time training to equip themselves for effective work at the clinics. One prerequisite is that the child psychiatrist should be prepared to devote a limited but definite amount of time to teaching. The question of there being a sufficient amount of psychologist's time might have to be considered. A major hurdle to be jumped is that of payment to the clinical assistant, whether when in training or afterwards, and I do not see that regional hospital boards will be ready to allot money for this purpose. The only way of getting over this difficulty would seem to be by asking a local health or education authority to second part-time to the child guidance clinic a selected doctor whom the authority is employing whole- or part-time as a member of its school medical officer staff.—I am, etc.,

Child Guidance Centre, West Bromwich. D. T. MACLAY.

SIR,—While willing to consider part-time attendance at a mental hospital and child-guidance clinic a practicable proposition for the married woman doctor for examination purposes, Dr. W. Warren (October 1, p. 1017) seems to feel that we, as mothers of young children, imagine ourselves to be suitable for child psychiatric work, for that reason alone. Surely he cannot really believe this? As I suggested in my letter of September 3 (p. 737), only those considered after a probationary term of work in a clinic to be suitable should be permitted to continue. Personal experience of bringing up children may be valuable to anyone working in any form of children's clinic, but I do not suggest that this would give the mother of young children any sort of scientific, clinical, or diagnostic training, but simply that it may make her *interested* in child psychiatry. Her only advantage over her colleagues is that she knows what it is like to be dealing with small children all day—and, if she still wants to know more after that, she really *must* be interested! And this, after all, is precisely what Dr. A. K. Graf in his original letter on the subject (August 20, p. 600) cited as one of the major difficulties in getting staff. Both Dr. Judith M. Waterlow and Dr. Susannah Davidson in letters on school phobia (October 1, p. 1016) mentioned grave shortage of psychiatric and other staff causing long waiting-lists in the clinics and subsequent delay in starting treatments in these cases.

Dr. Warren also says that much patience will be needed for a woman to remain in a junior position for double the normal time, if working part-time only. This is true, but surely for any mother a genuine interest in this type of work must be synonymous with being no longer a "career woman" *per se*. Having embarked upon producing a family must mean to her that she is prepared to bring them up herself and jettison her full-time career to do so. She knows she cannot have her cake and eat it, but wishes to be of some use in this understaffed field, in any capacity where she can learn at the same time.—I am, etc.,

Sutton Valence, Kent. BRIDGET ATTLEE.

Deaths from Drowning

SIR,—There is no doubt, as Dr. F. W. Woodruff writes (September 10, p. 798), that it is a great pity so many swimming-baths are closed in the winter. The usual reason is that the numbers attending do not justify the expense. But this does not seem reasonable when even in the winter the school swimming is sometimes limited to 20 minutes per school. Sometimes, too, there is the excuse that, although the water could be heated, the building is not suitable for keeping an adequately warmed air temperature in winter. It seems a great pity that a sport which could be enjoyed all the year round is limited to the better months. No one who has seen the pleasure and enthusiasm of the many children who go to the baths would wish this sport to be curtailed.

I agree with Dr. Charles Mills (September 24, p. 942) that the instruction of children in swimming is not always done with enough attention to safety. They are, as he writes, taught in smooth water without currents. They are therefore likely to be caught out in sea or river. In my opinion there is sometimes too much emphasis on swimming the back or front crawl. These are not easy strokes to swim in a rough sea because breathing is difficult. The breast stroke, on the other hand is a most seaworthy stroke for rough water, and

has the added advantage of giving better visibility, which is important in boating accidents or in approaching drowning persons. It is perhaps unfortunate that in Australia the breast stroke is no longer taught as a basic stroke. This is not to say that the front crawl has no safety aspects. It certainly has. It is a powerful stroke, and the horizontal position may enable the swimmer to make headway against a current which otherwise would defeat him. But more important than the stroke is the teaching of floating. Every child should know that perpendicular floating is possible without any expenditure of energy. This is one of the most valuable of all safety lessons. It gives confidence if the child knows that he is naturally buoyant provided he does not raise his arms. Drowning is basically lack of confidence.

Children should always be taught to swim parallel to the seashore. It should be explained to them that no swimmer, however strong, can swim against even a moderate tide. But, having mastered the basic rules for safety, the child should then swim for pure pleasure, not with any idea that he is learning a life-saving lesson. The comparison should not be to the life-saving of polio vaccination, as has been suggested. Fun is more important.—I am, etc.,

Chester. G. P. WHITWELL.

School Phobia

SIR,—All who are concerned with the well-being of children of school age will have been pleased to read your leading article (September 17, p. 848) on this almost epidemic condition which has developed in recent years in this and other countries. Some of your comments, however, would not seem to be justified either by experience or from reading the references quoted in the article. In particular I wonder what evidence there is for the statement that "child-guidance clinics tend to be so cluttered up with simple cases referred by school medical officers, which would have been perfectly well dealt with by a paediatrician." I can find nothing to support this in the most interesting article by Dr. John Apley and his colleagues,[1] though this is given as a reference for the phrase. Did such a situation exist, the remedy would lie in the hands of the clinic director, who should be able to indicate not only to school doctors but also to general practitioners, magistrates, probation officers, health visitors, social workers, teachers, and paediatricians the kind of child and family his clinic is best able to help.—I am, etc.,

Hassocks, Sussex. DENIS PIRRIE.

REFERENCE

[1] Apley, J., Philips, M., and Westmacott, I., *Brit. med. J.*, 1960, **1**, 191.

SIR,—In your interesting leading article (September 17, p. 848) you did not mention "word blindness" as one possible cause of "school phobia." In Denmark I understand this condition is taken very seriously in all schools, and it has been estimated that 10% of children suffer from it to a slight or greater degree. These children, often very intelligent, have great difficulty in spelling and writing and are labelled stupid, or idle, and are laughed at. Knud Hermann in his book[1] mentions that children will sometimes go to great lengths to avoid school. One for a long time managed to fake a temperature, and prepared to suffer being confined to bed rather than go to school.

The few educational people in this country to whom I have spoken have said that they have heard of it, but do not seem interested. The fact that it is so common in Denmark suggests that the condition may be missed in this country.—I am, etc.,

Oxford. MALCOLM DONALDSON.

[1] Hermann, K., *Reading Disability: A Medical Study of Word-blindness and Related Handicaps*, 1959. Based on *Om medfødt ordblindhed*, rev. by the author and trans. by P. G Aungle. Munksgaard, Copenhagen.

"Winkle-picker's" Disease

SIR,—It is difficult to accept that this condition (September 24, p. 944) can be identified as tenosynovitis of the synovial sheath of the long extensor tendon of the hallux, because in the words of *Gray's Anatomy*, page 653 of the 28th edition, the "sheath of the extensor hallucis longus is prolonged on to the base of the 1st metatarsal bone" and not any further distally.—I am, etc.,

St. George's Hospital, Lincoln. DAVID F. THOMAS.

SIR,—I am afraid that Mr. J. N. Wilson (September 24, p. 944) is barking up the wrong tree. He is obsessed, as most people are, by the theory that functional foot disabilities are caused by ill-fitting shoes. I keep reiterating that usually it is not shoes that deform feet, but feet that deform shoes. By his own showing, it is not the point of the shoe that is causing the trouble, but the rim of the shoe. This can be adjusted by the manufacturer. It is immaterial whether people have high heels, low heels, or cuban heels, provided that the shoes are a reasonable size and fit. Unless and until the medical profession advise and use my insoles no progress will be made. These insoles are described fully in *The Practitioner*.[1] They support the outer end of the metatarsal arch and enable the great toe to come down and function fully. When that happens, the remaining toes are given room to be used and there is no further trouble. I have old ladies, amongst others, who have been attending chiropodists for 20 years and more, but when they consistently use my insoles they do not need to avail themselves of the chiropodists' services. Chiropodists are well aware, when they remove corns, callosities, etc., that their clients will return with a fresh lot sooner or later.—I am, etc.,

Southgate N.14. W. SIMPSON.

REFERENCE

[1] Simpson, W., *Practitioner*, 1958, **181**, 336.

Nits at the Hairdresser's

SIR,—I was consulted recently by a hairdresser about what appeared to her to be a nit infestation (pediculosis capitis) on brushes used in hair-setting. I was able to confirm that they were heavily infested. The brushes are cylindrical, of bristle, with a wire spindle, and 4 cm. long by 2.2 cm. diameter. This brush goes inside a tube made usually of nylon. The bristles protrude through holes in the tube and the hair is twisted round the tubes and set under a dryer. The brushes, on this occasion, were not sterilized between one head and the next, but were put together in a tray. They were said to be put in a formalin sterilizer at the end of the day. The hairdresser noticed that brushes with nylon bristles were unaffected, even though intimately mixed with those

of natural bristle. The hairdresser has disposed of all bristle brushes, and has had no trouble, so far as I know, since.

It seems that hairdressers are more vulnerable than they used to be to this nuisance. Girls who are well paid and well dressed and who have a "hair-do" at the best local salon may well come from homes where several younger brothers and sisters are heavily infested with head-lice.

I would like to thank Dr. J. B. Kershaw (Medical Officer of Health to the Hinckley U.D.C.) for his advice. We both felt that hairdressers might be glad to know of this problem. We also felt that not much seemed to be known of the practical techniques in keeping brushes and combs clean when in busy use. Has anyone, for instance, any authoritative advice about the efficacy of the little sterilizing cabinet which one sees in most barbers' shops?—I am, etc.,

Hinckley, Leicestershire. J. K. WATERLOW.

Needled in One

SIR,—I came across this unusual case while doing a locum in Blackpool. The patient described how in the act of driving off from the first tee he suddenly felt a stabbing pain in the thigh. Thinking he had been stung, he showed me a red raised patch on the inner and upper aspect of the right thigh consistent with a sting. Thinking that the inflammation would best be subdued by penicillin, I was surprised when he came back in a couple of days saying that he thought he could feel something sticking in his leg like a needle. *X*-ray and subsequent operation revealed a needle one-and-a-half inches long embedded in the muscle of the thigh.

Being a tailor by trade, it would appear that he had the habit of parking his needles somewhere in the top of his trousers, and evidently one had decided to go for a run and finish up in the way described.—I am, etc.,

Blackpool. J. E. SWINBURNE-JONES.

Development of Live Polio Vaccine

SIR,—I have read the letter from Dr. D. E. Jeremiah (August 6, p. 468) concerning my article on "Historical Aspects of the Development of Live Virus Vaccine in Poliomyelitis" (July 9, p. 85). Dr. Jeremiah is mistaken if he thinks that, as a result of his letter, "We are confounded because we have heard reproach: shame hath covered our face"—as expressed so aptly by his more famous namesake. Because of the discovery which my colleagues, Dr. George Jervis and Mr. Thomas W. Norton, and I made 10 years ago, 85 million people throughout the world have now been effectively vaccinated against poliomyelitis. It therefore seems rather pathetic to find that to-day there is still a voice crying (in the wilderness, we hope) for "protection" against "individuals carrying out such trials on people who have not volunteered." Although such a coincidence is highly improbable, it would have been catastrophic indeed if it had been Dr. Jeremiah whose permission was sought in 1950 for vaccinating the first group of children with live attenuated poliomyelitis vaccine. He would have recoiled in horror then, as he is doing to-day, and as he probably would have done at the scientific endeavours of Jenner and Theiler or anyone else engaged in "so-called experimental trials."

There are experiments conducted in human beings which could be easily and more successfully undertaken in laboratory animals, and these should be condemned unequivocally by everyone. However, in his horrified reference to the discovery of live polio vaccine, Dr. Jeremiah "is confounded by the graven image," since the only price which the first group of children to receive the oral polio vaccine have paid for undergoing this illusionary danger in 1950 is the "protection" of numerous vaccinated subjects throughout the world who otherwise might have succumbed to the paralytic disease. Even though Dr. Jeremiah might think he was chosen, as was his glorious namesake, to be "battle ax and weapon of war," what he is attacking in his letter is not the depraved Babylon but the windmills of La Mancha.—I am, etc.,

Wistar Institute, Philadelphia 4, U.S.A. HILARY KOPROWSKI.

900 Million Units of Penicillin and Still Going Strong

SIR,—An American youth entered my consulting-room, complaining of headache. He had ridden a motor-cycle across Spain in the heat of August without wearing glasses. He could barely read half-way down an ordinary eye-chart for testing vision, but with glasses he could read the bottom line. On inquiring into his history I found he had had rheumatic fever 10 years ago and had taken 250,000 units of penicillin daily on almost every day since then. His father is a heart specialist in America, and when I questioned his father's approval he replied that perhaps his father was unduly cautious, but he approved of the treatment. Most of the penicillin had been taken orally, and my patient exhibited neither allergy nor mycotic infection, nor had he any other complaint than headache, which surely had nothing to do with penicillin.

I remember when there were only 30 grammes of penicillin in the world at the Sir William Dunn School of Pathology in Oxford in 1940. It has gone a long way since then.—I am, etc.,

Tangier. D. F. LITTLE.

POINTS FROM LETTERS

Effect of Physical Exercise on Alimentary Lipaemia

Dr. G. L. DAVIES (Bath) writes: Whilst the general principles on which the article by Dr. Harold Cohen and Miss Cissie Goldberg (August 13, p. 509) is based have no doubt occurred to many of us, I would like to add the observation that the great increase in coronary disease since the last war is, to my mind, connected with the great increase in motor traffic and the consequent decrease in bodily movement on the part of the population generally. . . . Since my partial retirement from practice a year or so ago I have walked many miles along country roads and have rarely met a single person on foot, whereas cars and motor-cycles seem to stand outside almost every cottage and council house. Even that formerly hard-working class, the farmer, rides all day on some motor vehicle or other, and young farmers will often use their tractors as a mode of conveyance for the few hundred yards which separate their farms from their cottages.

Correction.—We much regret that the letter by Mr. D. G. WILSON CLYNE in our issue for October 1 (p. 1020) was wrongly headed "Mental Health Tribunals" and wrongly made to refer to a letter by Dr. F. E. Graham-Bonnalie on this subject which appeared in our July 30 issue (p. 389). Mr. Wilson Clyne's letter in fact referred to the letter by Dr. Graham-Bonnalie published in our issue of September 17 (p. 861) on the subject of "Doctors' Letters" and was, of course, also concerned with the question of doctors' letters. We apologize for the confusion.

Obituary

J. M. MUNRO KERR, M.D., F.R.F.P.S., F.R.C.O.G.

Professor J. M. Munro Kerr, formerly Regius Professor of Midwifery in the University of Glasgow, and an ex-President of the Royal Faculty of Physicians and Surgeons of Glasgow, died on October 7 at Canterbury, where he had lived since 1935. He was 91 years of age.

John Martin Munro Kerr was born at Glasgow on December 5, 1868, the son of a shipowner, and was educated at Glasgow Academy and at the University of Glasgow, where he graduated M.B., C.M. in 1890. After holding the usual resident appointments, he decided to specialize in obstetrics and gynaecology, and studied for two years at the Rotunda Hospital, Dublin, and at Jena and Berlin. In 1895, at the age of 27, he was elected a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow. He proceeded to the M.D. in 1908, receiving a high commendation for his thesis. Munro Kerr was appointed visiting obstetric surgeon to the Royal Maternity Hospital, Glasgow, in 1900, and seven years later he became gynaecological surgeon to the Western Infirmary. In 1911 he was elected to the newly instituted Muirhead Chair of Midwifery and Gynaecology in the University of Glasgow and to the staff of the Royal Infirmary. Sixteen years later he succeeded the late Professor Murdoch Cameron as Regius Professor of Midwifery, resigning from this Chair in 1934, when the title of Emeritus Professor was conferred upon him. In the following year he received the honorary degree of LL.D. from the University of Glasgow.

[*Annan, Glasgow*

For forty years Munro Kerr was on the teaching staff of the University of Glasgow, and he did much to enhance the fame of the Glasgow medical school. His eminence as an obstetrician and gynaecologist was recognized both at home and abroad. As long ago as 1911 he was admitted an Honorary Fellow of the American Gynaecological Society, and he also received the Honorary Fellowship of the Royal Academy of Medicine in Ireland and the Edinburgh Obstetrical Society. Apart from his fame as a teacher, he was a well-known examiner, serving numerous universities in that capacity.

With the creation in 1929 of the British College of Obstetricians and Gynaecologists, of which he was a Founder Fellow, Munro Kerr was elected its first vice-president. In 1947, as one of the surviving signatories to the Articles of Association of the College, and to mark the grant of the Royal Charter of Incorporation in 1946, he was elected to the Honorary Fellowship. In the following year he delivered the William Meredith Fletcher Shaw Memorial Lecture at the College, taking for his subject the investigation and treatment of "borderline" cases of contracted pelvis. He was a member of the council of the College from 1929 to 1935; vice-president from 1929 to 1932; and trustee from 1929 to 1947. A tribute to his work and standing in his specialty was paid to him in November, 1950, a few days before his 82nd birthday, when Lord Webb-Johnson, as President of the Royal Society of Medicine, presented him with the first Blair-Bell medal of the society. At the ceremony it was said that Munro Kerr had adorned and embellished the profession for over 50 years, and during that time he had stimulated and inspired hundreds of students, undergraduate and postgraduate, and had earned the regard and affection of countless colleagues. It was the unanimous vote of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine that he should be the first recipient of the medal. He had previously been vice-president of the Section of Obstetrics and Gynaecology on several occasions and president in 1941–2.

Professor Munro Kerr was president of the Royal Faculty of Physicians and Surgeons of Glasgow from 1933 to 1936, and in 1956, in his 88th year, he delivered the inaugural William Hunter Memorial Lecture in the hall of the Faculty. The British Medical Association, too, saw in Munro Kerr a man of outstanding merit, and he accepted its invitation to hold office as a vice-president of the Section of Obstetrics and Gynaecology at the Annual Meeting held at Glasgow in 1922 and again at the Centenary Meeting of the Association in 1932. Two years later he served as the president of the Section. In 1934, also, he was awarded the Katherine Bishop Harman prize of the B.M.A. for his study of maternal mortality and morbidity.

Professor Munro Kerr's renowned book, *Operative Obstetrics*, was first published in 1908. The sixth edition, published in 1956, was taken over by Professor J. Chassar Moir, who in his introduction paid a warm tribute to the original author, saying that it was his store of clinical and "human" experience that gave Munro Kerr's teaching much of its unique character and authority. Munro Kerr was also the main author of the *Combined Textbook of Obstetrics and Gynaecology for Students and Practitioners*. First published in 1923, it reached a fourth edition in 1944, with many distinguished authors among its contributors.

Professor Munro Kerr was a man of great charm and good humour, and always approachable. Soon after his retirement he settled at Canterbury and became a popular medical figure in East Kent. During the second world war his knowledge and experience were of great value to the Kent and Canterbury Hospital, where he worked as medical superintendent. Although he gave up active practice many years ago, he maintained his interest in medical affairs into old age, contributing an article to this journal in 1951 on the use of radiography in determining the placental site.

Professor Munro Kerr, who was a widower, married the daughter of Mr. August Johanson, of Gothenburg, Sweden, in 1899. They had one son and three daughters.

V. B. G.-A. writes: Forty-eight years ago Glasgow was the Mecca of all obstetricians. Among these was myself and many others who clamoured to go round with Munro Kerr. In those days, as well as after the first great war, when I visited him again, his book and his teachings were famous throughout the Empire, for not only could he make his subject live, but he could lace every clinical lecture with pawky humour. Indeed, I think it gave him pleasure to meet anyone from the India of that period; for we, like him, knew all about the contracted outlet and osteomalacia—conditions which the dark places of the "Prof's" great city also supplied. He was the soul of generosity to all his suppliants, and I think nothing gave him so much joy as to entertain royally at the Union Club and fill his guests with port and lashings of usquebaugh. He was a wonderful host, and next to entertaining at his home was the joy of doing so in his yacht. Those were the days when he and I in our different localities were working out the joys and benefits of the lower-segment caesarean, and so it is nice to recall the great man's kindness when he wrote me asking whether he could quote our Calcutta results in the coming edition of his famous *Operative Midwifery*. He was indeed the G.O.M. of our specialty, and although not State-rewarded he possessed a greater prize—the love, admiration, and staunch loyalty of all those who knew and worked with him or heard him speak.

HENRY LAMB, *M.C.*, R.A., L.M.S.S.A.

Mr. Henry Lamb, who was an artist of renown, died on October 8, aged 77. As a student he turned from medicine to painting, but later he qualified as a doctor and served in the R.A.M.C. during the first world war.

Henry Taylor Lamb was the son of Sir Horace Lamb, F.R.S., professor of mathematics at the University of Manchester. From Manchester Grammar School he went on to study medicine at the university, but in the early years of this century he decided to become an artist and left Manchester to study in Paris and elsewhere. His talents soon gained him recognition, and his painting "Death of a Bretonne," painted in 1910, is now in the Tate Gallery, of which he was later to become a trustee. On the outbreak of the first world war he decided to complete his medical training at Guy's Hospital, and qualified L.M.S.S.A. in 1916. Thereafter he served as a battalion medical officer in France, Salonika, and Palestine, winning the M.C. A picture he painted in Salonika of an advanced dressing station is now in the Manchester City Art Gallery.

After the war Lamb returned to work as a professional artist, holding his first one-man exhibition in 1922. His work was not confined to any one type of subject, though most of the pictures he exhibited at the Royal Academy were portraits. Professor T. R. Elliott, F.R.S., who sat for his portrait to Mr. Lamb in 1953, said that every sitting with him was a pleasure, for he was an enthusiastic talker: this portrait now hangs in the library of University College Hospital Medical School.

During the second word war Mr. Lamb worked as an official war artist for the Army. Elected A.R.A. in 1940, he became an R.A. in 1949. The Tate Gallery has five of his paintings, including the famous portrait of his friend Lytton Strachey, and he is represented in many other art galleries throughout the country, including the Imperial War Museum.

G. H. THOMSON, M.B., Ch.B.

Dr. G. H. Thomson, who practised at Longtown in Cumberland for almost thirty years, died suddenly on October 2, at the age of 59. He was made a Fellow of the B.M.A. this year for his outstanding services to the Association.

George Hunter Thomson was born in Newcastle upon Tyne in 1901, and through his mother descended from Thomas Carlyle, the nineteenth-century historian. He received his medical education at Edinburgh University and graduated M.B., Ch.B., in 1923. After a resident hospital post in Darlington and a period in practice in Langholm, he became an assistant in a family practice in Glasgow. Shortly afterwards he bought the practice of Dr. Rankine in Longtown. He was soon appointed medical officer to the local isolation hospital, and when the Health Service began he became a part-time senior hospital medical officer at Longtown Hospital. His practice was a widely scattered one and called for physical endurance as well as for constant mental effort and initiative. During the second world war he served as medical officer to the 4th Battalion of the Border Regiment until he was invalided out of the Army after Dunkirk. He returned to his practice, which was enormously increased in size and in area by wartime conditions, and he continued to run it, often single-handed, until quite recently, when his health began to fail.

In addition to his heavy professional commitments he found time, as the busiest people do, to serve on innumerable committees. He was chairman of the Cumberland Division of the Border Counties Branch of the B.M.A. from 1941 to 1949, and he also served as president of the Branch from 1954 to 1956. He was very proud of receiving the Fellowship of the Association. For some years he was chairman of the Cumberland Executive Council and vice-chairman of the Cumberland Local Medical Committee. He was also a Justice of the Peace for the County of Cumberland.

Hunter Thomson was quiet and unassuming. At meetings he would listen to long-winded discussions with remarkable patience and then he would say: "What I think you are trying to say is . . .", and the problem would be solved, or at any rate nearer solution. In his earlier days he engaged actively in many sports and later was an enthusiastic observer of first-class cricket.

In 1929 he married Miss Anne Owen, of Edinburgh, who, with three daughters, survives him. Their sorrow is shared by a very great number of patients and friends.—T. McL. G.

W. G. BENDLE, M.B., B.S., F.R.C.S.Ed.

Dr. W. G. Bendle, formerly medical superintendent of Paddington Hospital, died at his home in Weymouth on August 27, aged 81.

William George Bendle was born at Frome, Somerset, on February 8, 1879. One of his great-uncles was the famous Benjamin Jesty, of Worth Matravers, Dorset, "who by his great strength of mind inoculated his wife and two sons with the cow-pox." He was educated at Frome Grammar School and at Wellingborough, and after training in engineering with the Great Western Railway he went out to Africa as a surveyor for the Central African Railway. Returning to England in 1906 he was able to follow his own desire and entered Durham University as a medical student, graduating M.B., B.S. in 1911. His student career was a distinguished one, for he passed all his examinations with honours and was awarded the Goyder scholarship in surgery and the Charlton scholarship in medicine. Among the hospital appointments he held were those of resident surgical officer at the Radcliffe Infirmary, Oxford, and resident surgeon at the Hull and Sculcoates Dispensary. Later he was medical officer in charge of Burcote House Military Hospital. In 1919 he was admitted to the Fellowship of the Royal College of Surgeons of Edinburgh. After working as an assistant in general practice at Headingley, Oxford, and Hayes, Middlesex, he became assistant medical superintendent of Paddington Hospital in 1921, and in the following year was appointed medical superintendent. He remained in that post until 1935, when he retired because of ill-health and went to live in Weymouth. During the second world war he was surgeon to the military hospital at Bovington Camp and to Portwey Hospital, Weymouth. For some years he was an examiner in surgery and gynaecology to the General Nursing Council.

A member of the B.M.A. all his professional life, Dr. Bendle was chairman of the Kensington Division in 1935. A past-president of the Paddington Medical Society, he was greatly respected by his colleagues, and those who had the privilege of his friendship knew him as a wise doctor and as a man of culture with many interests. His last illness was painful and distressing, but he bore it with exemplary patience and fortitude. When his right leg was amputated he refused to give in and was soon about again on crutches.

Dr. Bendle married in 1910 Dorothy Helen Lyon, daughter of the late James Lyon, of Tarlscough Hall, Lancashire, and she and their one son survive him.

D. G. SHIELDS, M.B.E., M.B., B.Ch.

Dr. D. G. Shields, who had practised at Wroxham, Norfolk, since 1928, died after an operation at Hill End Hospital, St. Albans, on September 15. He was 60 years of age.

A Norwich man, Daniel George Shields was born on June 3, 1900, and educated at the Norwich Grammar School, where he became head boy. Later he served with the Artists Rifles in the first world war, after which he went up to Corpus Christi College, Cambridge, and continued his medical education at St. Bartholomew's Hospital. Qualifying in 1925, he held house appointments at the Devonshire

Royal Hospital, Buxton, and at the Norfolk and Norwich Hospital. He graduated M.B., B.Ch. at Cambridge in 1927.

Entering partnership in Wroxham, he served the Broadlands area for over thirty years, making sailing his main relaxation. Shortly after his arrival he became medical officer of health to the Smallburgh rural district council, and during the second world war he was area medical officer to the Civil Defence organization, being appointed M.B.E. for his services.

A keen member of the B.M.A., he was chairman of the East Norfolk Division, which he represented at the Annual General Meeting for the past three years, and was president of the Norfolk Branch at the time of his death. The National Health Service gave scope to his organizing ability and genius for committee work, and he served faithfully and conscientiously on the Norfolk Executive Council and on the East Anglian Regional Hospital Board. For some years he was county medical officer to the British Red Cross Society and helped to organize the ambulance and sitting-car services for Norfolk.

R. C. B. writes: In spite of his many activities "Bobbie" Shields, as he was affectionately known to his many friends, found time to take a personal interest in local affairs, and his name will always be associated with the building of the Hoveton village hall, a model for any such hall in the country. His extensive practice has lost a careful and kindly counsellor, who gave of his very best, whilst his partners could never have wished for a more loyal or considerate colleague. The deep sympathy of his many friends and medical colleagues for his widow, daughter, and son was shown by the numbers who attended the funeral service at the parish church at Wroxham.

Vital Statistics

Smallpox in Visitor

Modified smallpox was diagnosed in a Dutch businessman who arrived at London Airport on October 3 by flight number BA 791 from Colombo, Ceylon. This man attended the casualty department of Charing Cross Hospital on the afternoon of October 5, when he complained of an irritating skin eruption. He was found to have a sparse rash and was admitted the same night to Long Reach Hospital, Dartford, where the clinical diagnosis was confirmed. The patient's illness has been mild and his progress satisfactory. Laboratory confirmation of the diagnosis has not yet been obtained. Specimens taken on October 6 have so far yielded negative results. The stage of development of the rash when seen on October 5 suggested that the patient may have been infectious from October 2. He is presumed to have acquired his infection in Malaya.

All persons who travelled by the same flight as the patient must be regarded as having been exposed to risk of infection. Persons known to have been in contact with the patient, either on the flight from Ceylon or subsequently, have been placed under surveillance and offered vaccination. Health authorities of other countries have been kept informed of the movements of persons in contact who have either travelled or made arrangements to travel abroad. Those who are known to have been in contact with the patient since his arrival in England fall into three broad categories: (*a*) individuals with whom he associated for private or business reasons during the period October 3–5; (*b*) some members of the staff and a few of the prisoners at Wormwood Scrubs Prison, which the patient visited on October 3; (*c*) members of the staff and some of the patients at Charing Cross Hospital, where the case was seen on the afternoon of October 5.

Pollution of Lincolnshire Coastal Waters

Bacteriological tests have shown that the sea water off some Lincolnshire beaches is being polluted. The accompanying table shows the results of tests carried out last July on sea water collected from beaches at Skegness, and from other beaches to the north of that town. All sewage from Skegness is treated at a modern works, and no untreated sewage is discharged into the sea. A possible cause of the pollution is a large holiday camp at Ingoldmells, with numerous caravan sites along the coast as far as Huttoft Bank. Alternatively, the pollution may come down the coast from possibly untreated discharge into the rivers Trent and Humber. Further samples will be taken from the same beaches during the winter months when the holiday camp and caravan sites are closed. The Spilsby Rural District Council has recently approved a new sewerage scheme for the village of Ingoldmells and adjoining camp sites at a cost of £361,000. For these details we are indebted to Dr. A. LOFTUS, medical officer of health of Skegness and Alford Urban Districts and Spilsby Rural District.

Beaches Sampled	Coliform Bacilli per 100 ml.	*E. coli* per 100 ml.
Skegness U.D.C.:		
Southern beach	0	0
Central ,,	500	500
Northern ,,	1,600	900
,, boundary	18,000+	9,000
Under pier near northern beach	18,000+	18,000+
Ingoldmells:		
South beach	16,000	5,500
Central ,,	900	130
Northern ,,	1,700	450
Chapel St. Leonards:		
Chapel Pullover	130	130
Anderby Creek	130	50
Huttoft Bank	1,100	800

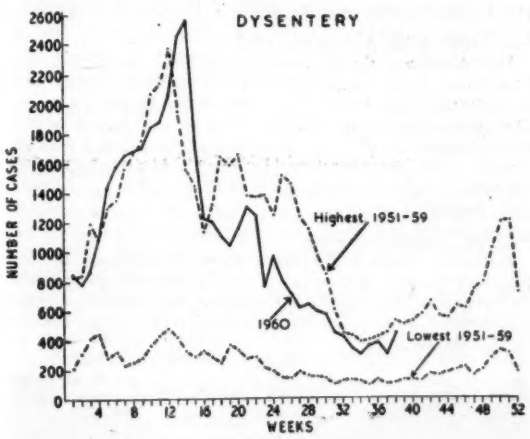
Infectious Diseases

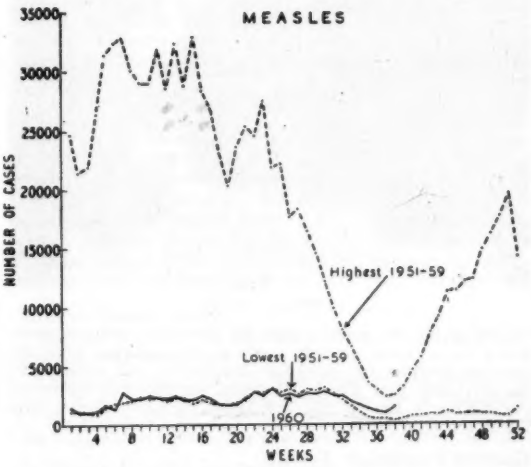
Areas where the numbers of notifications were high in the latest two weeks for which figures are available.

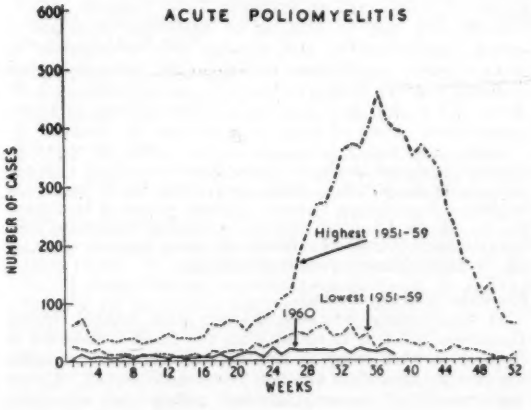
	Week Ending Sept. 24	Oct. 1
Measles		
Lancashire	627	**677**
Burnley C.B.	44	**97**
Liverpool C.B.	79	**91**
Acute Poliomyelitis		
London	1	**7**
Islington	0	**5**
Dysentery		
Essex	10	**41**
Thurrock U.D.	1	**21**
Kent	23	**51**
Tonbridge U.D.	2	**15**
London	86	**64**
Finsbury	14	**22**
Staffordshire	5	**21**
Newcastle-under-Lyme R.D.	0	**19**
Yorkshire West Riding	74	**69**
Leeds C.B.	23	**28**
Glasgow	75	**142**
Food Poisoning		
Devonshire	12	**12**
Exeter C.B.	7	**11**
Lancashire	55	**68**
Liverpool C.B.	31	**21**
Kirkby U.D.	0	**21**
Surrey	8	**26**
Carshalton U.D.	0	**21**
Diphtheria		
Devonshire	1	**2**
Plymouth C.B.	1	**2**

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1951–9 are shown thus ------, the figures for 1960 thus ———. Except for the curves showing notifications in 1960, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **September 24** (No. 38) and corresponding week 1959.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	3	0	1	0	1	6	3	1	0	2
Dysentery	434	86	108	9	4	529	62	195	1	2
Encephalitis, acute	0	0		0		3	0		0	
Enteric fever:										
Typhoid	6	2	0	0		4	2	1	3	
Paratyphoid	9	0	0	0		18	0	0	0	8 (B)
Food-poisoning	240	28	26	3		343	34	22	2	
Infective enteritis or diarrhoea under 2 years				16	33				18	72
Measles*	1,501	48	59	4	2	687	20	14	20	14
Meningococcal infection	20	0	6	0		17	1	9	1	
Ophthalmia neonatorum	15	0	3	0		29	1	5	0	
Pneumonia†	139	14	86	1		132	10	109	2	
Poliomyelitis, acute:										
Paralytic	3	1	1	} 1		{ 22	3	0	} 1	
Non-paralytic	5	0	1			{ 13	2	2		
Puerperal fever§	158	30	12	1		187	30	7	1	
Scarlet fever	275	14	43	13	12	531	37	80	14	15
Tuberculosis:										
Respiratory	357	41	61	13		440	61	56	16	
Non-respiratory	63	6	23	2		48	2	8	2	
Whooping-cough	1,132	102	115	14	29	784	41	79	10	29

DEATHS	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	2	0		0		0	0		0	
Encephalitis, acute		1			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	5	0	2	1	0	3	0	1	1	2
Influenza	6	0	0	1	0	5	0	0	1	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	320	29	15	15	3	334	28	14	14	0
Poliomyelitis, acute	0	0		0	0	3	1		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	} 50	{ 0	2	1	4	} 50	{ 1	2	1	3
Non-respiratory		0	0	0	1		0	1	0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	293	25	25	9	6	260	27	33	8	8
Deaths (excluding stillbirths)	8,950	713	508	117	142	7,931	662	523	103	108
LIVE BIRTHS	15,064	1300	1008	306	299	14,046	1263	887	259	313
STILLBIRTHS	306	24	23			296	26	16		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Tropical Medicine Research Board

The Medical Research Council announced in their last annual report that they had decided to establish a Tropical Medicine Research Board to advise them on the promotion and co-ordination of all research in this field. The membership of the Board has now been decided and is as follows:

Sir HAROLD HIMSWORTH, F.R.S. (*chairman*), Professor A. C. FRAZER (*vice-chairman*), Brigadier Sir JOHN BOYD, F.R.S., Professor P. C. C. GARNHAM, Professor W. E. KERSHAW, Dr. R. LEWTHWAITE, Professor G. MACDONALD, Professor B. G. MAEGRAITH, Professor B. S. PLATT, Professor M. L. ROSENHEIM, Mr. H. J. SEDDON, Professor E. T. C. SPOONER, Professor A. W. WOODRUFF, Dr. B. S. LUSH (*secretary*). The Chief Medical Officer and the head of the research department of the Colonial Office have been appointed assessors on the Board and two assessors have been nominated by the Secretary of State for Commonwealth Relations.

Medical Research Council Appointments

The Earl of LIMERICK has been reappointed as chairman of the Medical Research Council, while Dr. E. F. COLLINGWOOD, Sc.D., replaces Sir GEOFFREY VICKERS as treasurer. The Council's new scientific members are Professor T. CRAWFORD (professor of pathology, St. George's Hospital Medical School, London) and Professor W. M. MILLAR (Coombie-Ross professor of mental health, Aberdeen University). They replace Professor G. PAYLING WRIGHT and Dr. J. D. N. HILL, who are retiring after the normal four-year term of office. All these appointments date from October 1.

"Current Medical Research"

Current Medical Research, which has just been issued, is a reprint of the articles contained in the Medical Research Council's annual report for 1958–9. These are brief reviews of the more important findings of medical or biological research on selected subjects. (H.M.S.O., price 3s. 6d. net.)

Commission of Neuroanaesthesia

The inaugural session of the Commission of Neuroanaesthesia was held on July 9. In his inaugural address Dr. L. VAN BOGAERT, president of the World Federation of Neurology, said that the Commission's aim was to give those who practise anaesthesia an opportunity to increase their contacts with other neurological disciplines.

Those who are interested in the problems of neuroanaesthesia may apply to the secretaries of the Commission. They are Professor G. VOURC'H, 54 Rue Faubourg St. Honoré, Paris 8, France, for the eastern hemisphere, and Dr. H. R. TERRY, jun., Department of Anesthesia, Mayo Clinic, Rochester, Minn., U.S.A., for the western hemisphere. The joint secretary is Dr. A. SOETENS, Institut Bunge, 59 rue Philippe Williot, Berchem-Antwerp, Belgium. The Commission's British representative is Dr. A. J. H. HEWER.

Argentinian Association of Neurosurgeons

The newly formed Asociación Argentina de Neurocirugía will promote neurological research and facilitate the exchange of ideas between neurosurgeons. It will also grant fellowships on the results of national and international competitions. Dr. JUAN ALBERTENGO (Rosario) is the president, and Dr. A. D. KAPLAN (Buenos Aires) the secretary. The address (temporary) is 674 Larrea, Piso 1, Buenos Aires.

Lalor Foundation Grants

The Lalor Foundation, U.S.A., is offering a programme of awards for 1961 for research on the fundamental biochemical and physiological mechanisms concerned with fertility and the early stages of reproduction in various forms of life. A number of these awards may be granted to nationals other than U.S. citizens, usually under the condition that the award-holder's work shall be conducted at an American institution. Details may be obtained from the Lalor Foundation, 4400 Lancaster Pike, Wilmington 5, Delaware, U.S.A., to which applications should be returned by January 16, 1961. Notification of appointment will be on or before March 15.

Northern Ireland Mental Health Conference

A conference on "Planning for Mental Health" was held at the Queen's University, Belfast, from September 27 to 29 and was sponsored by the Northern Ireland General Health Services Board, the Northern Ireland Hospitals Authority, the Association of Health Committees of Northern Ireland, and the Association of Welfare Committees of Northern Ireland, with the support of the Ministry of Health and Local Government and the Queen's University of Belfast.

Van Meter Prize Award for 1961

The American Goiter Association, Inc., is offering the Van Meter Prize Award of $300 for the best original and unpublished essay on "Goiter—Especially its Basic Cause." The studies so submitted may relate to any aspect of the thyroid gland in all of its functions in health and disease. Details from the Secretary, Dr. J. C. MCCLINTOCK, 702 Madison Avenue, Albany 8, New York, U.S.A. Closing date, January 1.

National Spastics Society

Daresbury Hall, a Georgian mansion equipped by the National Spastics Society at a cost of £66,000 as a home for severely handicapped adult spastics, was formally opened last month. It is the twelfth national centre to be opened by the Society.

Daresbury Hall.

It will eventually house 21 men and 24 women, with accommodation for a further eight in a villa in the grounds. There are extensive facilities for recreation, handicrafts, and occupational therapy. The Rev. Charles Dodgson was rector of Daresbury Parish Church, and his son, best known as Lewis Carroll, often visited the Hall.

Gairdner Foundation Awards

The Gairdner Foundation of America has awarded prizes of $5,000 each to Professor J. MCMICHAEL, F.R.S., "as the first man in England to apply the technique of cardiac catheterization and through this investigation to make a major contribution leading to the fuller diagnostic accuracy required in heart surgery"; and to Professor J. H. BURN, F.R.S., for his "outstanding contributions to knowledge of the action of drugs in cardiovascular disease."

Similar prizes have been awarded to four Americans: Dr. J. H. GIBBON (professor of surgery and director of surgical research, Jefferson Medical College, Philadelphia); Dr. W. F. HAMILTON (professor of physiology, Georgia University School of Medicine); Dr. K. MEYER (dean of medicine, Columbia University, New York); and Dr. A. R. RICH (Baxley professor emeritus of pathology, Johns Hopkins University, Baltimore).

Multiple Sclerosis Society

In the Multiple Sclerosis Society's *Sixth Annual Report, December, 1959*, it is shown that the funds committed to research in 1958 stood at £20,254, while in the year under review they more than doubled to stand at £45,115. Among the aspects of research covered during the year were

geomedical surveys; basic research on myelin; immunological problems; social and clinical problems; and work on the auto-immune hypothesis of the aetiology of multiple sclerosis.

Chartered Society of Physiotherapy

Professor Ruth E. M. Bowden has been elected to the chairmanship of the Society in succession to Sir Harold Boldero, who is retiring.

Marriage Guidance Council

The new headquarters of the Marriage Guidance Council were officially opened at 58 Queen Anne Street, London W.1, by the Home Secretary, Mr. R. A. Butler, on October 4. The building was previously occupied by the Royal College of Obstetricians and Gynaecologists.

Christmas Cards

The Muscular Dystrophy Group has a series of cards at 2s. 6d. for six, obtainable from the Group at 26 Borough High Street, London S.E.1. (Tel. HOP 2324.)

The cards of the Invalid Children's Aid Association range in price down from 18s., 9s., 8s., and 5s. to 4s. a dozen, the 4d. card showing a small garlanded donkey with two cherubs. From the Appeals Secretary (or local office), I.C.A.A., 4 Palace Gate, London W.8.

The National Association for Mental Health has a series of cards at 9s. 6d., 7s. 6d., 6s. 6d., and 4s. 6d. a dozen, and is also offering a packet of 18 assorted cards for 10s. They are obtainable from the N.A.M.H., 39 Queen Anne Street, London W.1.

The National Deaf Children's Society card features a little girl with robin and snowballs and costs 3s. 6d. for six, including envelopes and postage, from the N.D.C.S., 31 Gloucester Place, London W.1.

The National Marriage Guidance Council's cards—"Family cards for a family cause"—include, "The Stork Family" by Eric Hosking at 6s. a dozen. There are other sets at 9s. and 4s. a dozen from N.M.G.C., 58 Queen Anne Street, London W.1.

Hospitals' Symphony Orchestra

The Hospitals' Symphony Orchestra has vacancies in all string sections and in some of the wind and brass sections. It meets on Mondays at 7.30 p.m. in St. Thomas House, Lambeth Palace Road, London S.E.1. The secretary—Miss M. A. Whipp, South-Western Hospital, London Road, London S.W.9 (BRI 7466)—will be pleased to answer inquiries about the orchestra.

Medical Golfing Society

The winners at the Medical Golfing Society's autumn meeting were as follows:

Lindsay-Rea Cup, Dr. L. J. Rae; *Bathurst Cup*, Dr. S. Pope and Mr. F. G. Ward; *Canny Ryall Cup*, Dr. P. Hargrove; *Creasy Salver*, Mr. H. W. Burge; *Milsom Rees Cup*, Dr. M. J. Healy; *Gordon Watson Cup (Veterans)*, Dr. G. H. C. Harding.

St. Mary's Hospital Medical School

Dr. G. B. Mitchell-Heggs has been appointed Dean of the Medical School with effect from October 1, in succession to Mr. A. G. Cross.

Games for the Disabled

Great Britain came second to Italy out of 21 countries in the Games for the disabled recently held in Rome.

Change of Title

The *Manchester University Medical School Gazette* has changed its title to the *Manchester Medical Gazette*.

"Family Doctor"

The October issue of *Family Doctor* is now available, price 1s. 6d. It contains articles on stress in executives by Mr. H. Beric Wright, on schizophrenia by Dr. H. J. Brawn Miller, on living in a wheel-chair by Dr. N. P. R. Clyde, and on coronary disease by Sir Heneage Ogilvie.

Grants, Gifts, and Bequests

The Brown Memorial Trust has made a grant of £20,000 towards the building and equipping of a leper hospital at Malamulo Mission, Nyasaland. The Trust administers the £230,000 fortune left by the Brown family of Mlanje, who were tea-planters.

The U.S. National Institute of Health has made a grant of $100,000 to Professor Leo Sachs, of the Weizmann Institute of Science, Israel, for further research on viruses in cancer.

In Brief

The Royal Flying Doctor Service has launched a service in Tasmania, and will serve many areas otherwise isolated by rugged bush country or water.

Three linear accelerators, each costing about £50,000, have been ordered by the Ministry of Health. They will be used at Cookridge Hospital, Leeds; Whitchurch Hospital, Cardiff; and the Christie Hospital and Holt Radium Institute, Manchester.

The National Library of Medicine in the United States plans to plant in the grounds of its new building in Bethesda a slip from the plane tree on the Dodecanese island of Cos, under whose shade Hippocrates is reputed to have taught his students.

People in the News

Mr. Austin Concanon and Dr. R. E. Angel have been invited on a lecture and demonstration tour by the Asociacion de Obstetricia y Ginecologia, Barcelona, and the Institute of Obstetrics and Gynaecology, Madrid.

Dr. R. Bentley, Ph.D., formerly of the staff of the National Institute for Medical Research, Mill Hill, has been made professor of biochemistry and nutrition at the University of Pittsburg, U.S.A.

Dr. Raymond Greene has been created a Chevalier of the Legion of Honour by the President of the French Republic.

COMING EVENTS

B.B.C. Sound.—Sir Henry Dale, O.M., F.R.S.: "I Remember," a programme of scientific reminiscences. October 16, 10.10 p.m.

Society for the Study of Addiction: Annual Dinner, October 17, 7 p.m., Rembrandt Rooms, Thurloe Place, London S.W.7. Principal guest: Mr. Arthur Dickson Wright. Tickets (25s.) from Dr. Ellis Stungo, 93 Harley Street, London W.1.

Harveian Oration. — Sir Francis Fraser: "The Challenge to the Medical Profession," October 18, 3 p.m., Royal College of Physicians, Pall Mall East, London S.W.1.

Abortion Law Reform Association, — Annual public meeting, October 25, 7.15 p.m., Conway Hall, Red Lion Square, Holborn, London W.C.1. Speaker: Dr. G. I. M. Swyer, "Oral Contraception."

Thomas Vicary Lecture, R.C.S. Eng.—Dr. Cuthbert E. Dukes, "Genetics in Relation to Surgery: a Historical Review," October 27, 5 p.m., at the College. Tea, 4.30 p.m.

Institute of Dermatology.—Semi-permanent exhibitions are available during the autumn term. Until October 27 "Normal Skin" by Dr. H. Haber, St. John's Hospital for Diseases of the Skin, Lisle Street, Leicester Square, London W.C.2.

Association of Industrial Medical Officers.—91st meeting, Royal College of Surgeons of England, October 28, Royal Eye Hospital, London, October 29. Details from the Secretary, 47 Lincoln's Inn Fields, London W.C.2.

William Blair-Bell Memorial Lecture, R.C.O.G.—October 28, 5 p.m., Mr. Ian MacGillivray: "Hypertension in Pregnancy and its Consequences," Nuffield Hall, Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent's Park, London N.W.1. Tickets not required.

Symposium on "Asthma." — University of Edinburgh, November 2; chairman, Professor J. Crofton. Details from Chest and Heart Association, Scottish Branch, 65 Castle Street, Edinburgh 2.

London School of Hygiene and Tropical Medicine.—School Association dinner, November 4, 7 for 7.30, Waldorf Hotel, Aldwych, London W.C.2. (Dinner jackets.) Tickets, 30s. each, exclusive of drinks. Guests: Sir PHILIP MANSON-BAHR and Lady MANSON-BAHR.

Association of Anaesthetists of Great Britain and Ireland.—Annual meeting, Royal College of Surgeons of England, November 4, 5. Details from the Secretary, 47 Lincoln's Inn Fields, London W.C.2.

Charité, Berlin.—The Charité will celebrate its 250th anniversary in Berlin from November 6 to 19, in connexion with the 150th anniversary of the Humboldt University. Details from Dr. DAGOBERT MÜLLER, 20–21 Schumannstrasse, Berlin N.4, Germany.

University of Montreal: Department of Psychiatry.—International symposium: "The Extrapyramidal System and Neuroleptics," November 17, 18, 19. Details from Dr. J.-M. BORDELEAU, Department of Psychiatry, University of Montreal, Montreal, Canada.

Hungarian Congress of Internal Medicine.—Budapest, November 23–26. Main subject, "Pathology of the Kidney." Details from Congress Secretariat, Second Department of Medicine, University Medical School of Budapest, VIII. Szentkirályi u. 46, Hungary.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

*The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.*1.

BRITISH JOURNAL OF OPHTHALMOLOGY

Drainage Channels in the Trabecular Wall of Schlemm's Canal. J. S. Speakman.
Error and Discovery in Fundus Disease. I. C. Michaelson.
Toxoplasmosis: Serological Studies in Patients with Chorio-retinitis in Nigeria. H. A. Iverson, M. D. Hursh, and A. Lewis.
Non-Traumatic Dialysis in the Young. M. E. Cameron.
A Survey of Patients Using Spectacle Magnifiers. G. S. Willetts.
Orbital Angioma Diagnosed by Phlebography. H. E. Hobbs, G. du Boulay, and R. E. Davis.
Peritoneal Graft in Extremely Retracted Conjunctival Sac. S. Erbakan.
Segmental Lesions of the Retinal Arteries. R. K. Blach.
Myxoedema with Enophthalmos. R. J. Schen.
Meningocoele of the Optic Disc. P. Wright.
Ocular Complications in Molluscum Contagiosum. S. P. Mathur.
Unilateral Corectopia. S. P. Mathur.
Correspondence.
Notes.

Volume 44, No. 9. (Monthly; £6 annually. With *Ophthalmic Literature* and Index, £9.)

BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE

Observer Error and Variation in the Interpretation of Electrocardiograms in an Epidemiological Study of Coronary Heart Disease. R. M. Acheson.
Climate, Air Pollution, and Mortality. F. C. Stallybrass.
Anencephaly in Univular Twins. F. C. Stallybrass.
Mortality from Cerebrovascular Accidents and Hypertension in the Republic of Ireland. R. M. Acheson.
Society for Social Medicine.

Volume 14, No. 3. (Quarterly; £3 annually.)

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, October 17

●HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, E.C., 7 for 7.30 p.m., dinner-meeting. Presidential address by Dr. Gordon B. Mitchell-Heggs: Skin Deep.
POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. John Marshall: Present Status of Therapy in Cerebrovascular Disease.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Erasmus Wilson Demonstration by Dr. A. R. Currie: Modern Aspects of Thyroid Pathology.

Tuesday, October 18

LEEDS NEUROLOGICAL SCIENCES COLLOQUIUM, 1960.—At Littlewood Hall, General Infirmary at Leeds, 5.15 p.m., Dr. J. D. Spillance: New Dimensions in Neurology.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. J. D. S. Cameron: Some Aspects of Hepatic Disease.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Lecture Theatre, Wright-Fleming Institute, 5 p.m., Dr. G. Mitchell-Heggs: Pruritus Vulvae.
SOCIETY FOR THE STUDY OF ADDICTION.—At 11 Chandos Street, London W., 8 p.m., Dr. Abraham Wilker (Kentucky, U.S.A.): Nature of Addiction and Habituation.
UNIVERSITY COLLEGE LONDON.—At Anatomy Theatre, Gower Street, W.C., 1.15 p.m., Dr. H. Kalmus: Biology of Fighting.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. G. A. D. Gordon: Stereotaxis.

Wednesday, October 19

BRITISH GERIATRICS SOCIETY: SOUTH WALES GROUP.—At Welsh Regional Hospital Board, Temple of Peace and Health, Cathays Park, Cardiff, 8 p.m., open meeting, Dr. J. H. Sheldon: Falls and the Elderly.
CAMBRIDGE MEDICAL SOCIETY.—At Owen Webb House, 1 Gresham Road, Cambridge, 8.30 p.m., B.M.A. Lecture by Dr. L. S. Penrose, F.R.S.: Mongolism.
HARVEIAN SOCIETY OF LONDON.—At Medical Society of London, 8.15 p.m., Dr. John Marshall, Dr. R. A. Beaver, and Dr. J. B. L. Howell: Symposium on Management of Respiratory Emergencies.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. A. Tickner: Biochemistry of Skin Diseases.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. V. H. Springett: Tuberculosis Epidemiology and Methods of Control.
INSTITUTE OF UROLOGY.—At 10 Henrietta Street, London W.C., 4.30 for 5 p.m., Dr. A. H. Harkness: Non-gonococcal Urethritis.
●LEEDS UNIVERSITY.—At General Infirmary at Leeds, (1) 5 p.m., Mr. H. Agar: Irregular Bleeding at Climacteric. (2) 6 p.m., Mr. G. W. Theobald: Significance of Antenatal Clinics and Antenatal Beds.
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8 for 8.30 p.m., talk by Mrs. Monica Jackson on her experiences with the Women's Expedition to the Himalayas, illustrated with colour photographs.
●MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 7 for 7.30 p.m., annual dinner. 8.45 p.m., address by Professor M. Stacey, F.R.S.: Alchemy—Ancient and Modern.
POSTGRADUATE MEDICAL SCHOOL.—2 p.m., Dr. K. Lowe: Tests of Renal Function.
ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—3.30 p.m., Mr. Eric Samuel: Mechanical Syndromes following Partial Gastrectomy.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—5 p.m., Bengué Memorial Award Lecture by Dr. W. A. R. Thomson: Doctors, Drugs, and Diseases.
SOCIETY OF APOTHECARIES OF LONDON.—5.30 p.m., Joseph Strickland Goodall Memorial Lecture by Mr T. Holmes Sellors: The Evolution of Intracardiac Surgery.
WILLESDEN GENERAL HOSPITAL MEDICAL SOCIETY.—At Department of Physical Medicine, Willesden General Hospital, 8.30 p.m., Dr. Frances Gardner: The Management of Hypertension.

Thursday, October 20

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., ordinary meeting, followed by Presidential Address by Dr. J. W. D. Bull: History of Neuroradiology.
BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Senate House, 5.30 p.m., Professor C. H. Waddington: Significance of Developmental Biology.
GUTHRIE SOCIETY.—At Westminster Medical School, 8 p.m., Dr. W. D Hoskins: Development of the English House.
LIVERPOOL MEDICAL INSTITUTION.—Pathological meeting. Professor D. H. Collins: Dysplasias and False Tumours of Bone.
MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Staff House, Manchester University, 7.45 for 8 p.m., Presidential Address by Dr. J. Sneddon.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Moynihan Lecture by Professor J. F. Nuboer: Recurrent Peptic Ulcer after Gastrectomy.
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—7.30 p.m., film show by Dr. Telford Work: Kyasanur Forest Disease in India.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Sir Paul Mallinson: postgraduate demonstration in psychiatry.

Friday, October 21

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. C. D. Calnan: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—3.30 p.m., clinical discussion for general practitioners. Miss E. Whetnall: The Deaf Child.
KENT AND CANTERBURY HOSPITAL.—8 p.m., clinical meeting.
MANCHESTER MEDICAL SOCIETY: SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre, Medical School, Manchester University, 8.30 for 9 p.m., Dr. M. Balint: Examination by the Patient.
POSTGRADUATE MEDICAL SCHOOL.—(1) 10 a.m., Dr. B. G. B. Lucas: Physiological Aspects of Anaesthesia. (2) 4 p.m., Dr. J. F. Goodwin: Cardiomyopathy.
ROYAL SOCIETY OF HEALTH.—At Council House, Bristol, 10 a.m., symposium by Dr. P. W. Bothwell, Dr. A. McDiarmid, Ph.D., D.Sc., M.R.C.V.S., and Dr. J. F. Skone: Recent Studies of Human and Animal Brucellosis: Prospects for its Control in the United Kingdom.

Saturday, October 22

BIOCHEMICAL SOCIETY.—At National Institute for Medical Research, Mill Hill, London N.W., 10.25 a.m., 399th meeting.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Hudson.—On October 1, 1960, at Park House Nursing Home, Liverpool, to Dr. and Mrs. Donald C. Hudson, Beechwood, Ruff Lane, Ormskirk, Lancs, a son.
Wisdom.—On September 22, 1960, at 3 Woodstock Road, Strood, Kent, to Drs. Charlotte (formerly Hartstein) and Anthony Wisdom, a third child—Michael Paul Nicholas.

DEATHS

Ferguson.—On September 22, 1960, at Studland Bay, Montgomery Du Bois Ferguson, O.B.E., M.D., D.P.H., of Farnham, Surrey, late of York.
Grant.—On September 16, 1960, at Dykesfield House, Burgh-by-Sands, Carlisle, Cumberland, George Osmond Grant, M.B., Ch.B.
Hunter.—On September 23, 1960, Mark Oliver Hunter, M.R.C.S., L.R.C.P., of 5 Chester Gate, Regent's Park, London N.W., aged 87.
MacIntyre.—On September 23, 1960, at his daughter's home, Carshalton Beeches, Surrey, Eneas John MacIntyre, M.D., D.P.H., of Rustington, Sussex, formerly of Cheam, Surrey, aged 62.
Moffett.—On September 23, 1960, in Birmingham, Warwicks, Elizabeth Jane Moffett, M.D., aged 93.
Phillips.—On September 16, 1960, at 108 Grosvenor Square, Rondebosch, South Africa, John Alfred Steele Phillips, C.I.E., L.R.C.P.S.Ed., L.R.F.P.S., D.P.H., Colonel, I.M.S., retired, late of Fowey, Cornwall, aged 77.
Read.—On September 22, 1960, at Exeter City Hospital, William Dunstan Boileau Read, B.M., B.Ch., Lieutenant-Colonel, I.M.S., retired.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Silver for Smoking

Q.—*Anti-smoking tablets containing silver acetate 6 mg. have been recommended in the following dosage: one tablet on arising and one tablet taken after each meal for several weeks. Are these tablets toxic in the dose stated?*

A.—It is improbable that these tablets would have any toxic effects in the usual sense of the term. The only danger would be the development of argyria if the tablets were taken for a long time. When silver salts are taken by mouth most of the silver passes through the alimentary canal unabsorbed. A minute amount of silver is absorbed and this is thrown down as tiny granules in the connective tissue of the body, where it gives rise to the characteristic pigmentation known as argyria. Once the silver is deposited it remains embedded in the tissues and the pigmentation is permanent. Apart from this pigmentation, toxic effects from silver salts are rare unless very large doses are taken.

The manufacturers of the tablets recommend a course of several weeks and state that the amount of silver absorbed during this period is far below the amount which would produce argyria. This is probably true so far as generalized pigmentation is concerned, but it is possible that sucking three or four tablets daily for several weeks might cause local pigmentation of the buccal mucosa. The smoker should certainly be warned that the tablets should not be taken indefinitely and also that repeated courses are as likely to cause pigmentation as prolonged use over a continuous period.

Sterilizing Insulin Syringes

Q.—*Is a solution of liquor boracis et formaldehydi suitable for sterilizing syringes for insulin injections? Bacteriologists and diabetic physicians seem to differ on the efficacy of spirit.*

A.—This solution is unsuitable for syringes. It was recommended in this column[1] for suture needles, and it may also be used for scalpels, Cheatle forceps, and other instruments. It is unsuitable for syringes both because the chemical sterilization of an assembled syringe, particularly of Record type, is difficult or impossible and because thorough washing would be necessary before the syringe was fit for use.

The diabetic's personal insulin syringe stands altogether apart from syringes used for other purposes. Since it is never used by anyone but the patient himself, there is no risk of transmitting infection from other people. Provided that it is protected against contamination from extraneous sources by ordinarily careful handling, it need only be sterilized at long intervals. If some kind of germicidal solution is preferred, the spirit in which such syringes are often kept in a metal case seems adequate for such a purpose.

References

1 *Brit. med. J.*, 1959, 2, 1033.

Recurrent Colic after Cholecystectomy

Q.—*A patient who has had a cholecystectomy, and is on a reduced fat diet, gets a passing attack of colic every two to three months. What is the explanation of this, and can anything be done?*

A.—There may be several explanations for recurrent colic after cholecystectomy. The most obvious possibility is that a stone is still present in the duct, which would tend to give recurrent colic followed by jaundice. This possibility might be excluded by intravenous cholangiography, when the common bile duct can sometimes be visualized and foreign bodies demonstrated. A second possibility is that pain is due to some type of biliary dyskinesia with recurrent spasm of the common duct or of the sphincter of Oddi. Again, intravenous cholangiography should be undertaken to exclude any organic obstruction, and antispasmodics, such as belladonna derivatives or one of the newer anticholinergic drugs, should be tried to see if they control the condition. Bile-duct stricture and recurrent cholangiohepatitis are rather unlikely, since these conditions are characterized by jaundice and by bouts of fever with shivering attacks. A last possibility is that an associated recurrent pancreatitis is present which produces a pain similar to biliary colic. In this eventuality it would be worth while having a plain abdominal *x*-ray to see if any calcification is present, and, if symptoms persisted, undertaking pancreatic function tests. If symptoms continued to be severe a further laparotomy might well be necessary to explore the common duct and to palpate the pancreas, and if no organic disease was found sphincterotomy might effect some improvement.

Genital Disproportion

Q.—*A small man is married to a large woman and they are unable to achieve adequate coitus because of their disproportionate size. Erection and ejaculation are normal. Seminal analysis, carried out before marriage, was normal. Is there any hormone therapy which would stimulate growth in this man without impairing his fertility?*

A.—From the fact that the patient has normal erection and ejaculation and produces normal seminal fluid, it must be concluded that there can be no endocrine deficiency. The smallness of genital development should be regarded as within the normal range of biological variation and evidently is in keeping with his small stature. There is no prospect of stimulating further genital growth by any kind of hormone preparation. In particular, intensive androgen therapy could be expected only to lead to arrest of spermatogenesis.

Risk of Further Subarachnoid Haemorrhage

Q.—*What is the risk of a further haemorrhage in a man aged 37 who has made an excellent recovery from a subarachnoid haemorrhage?*

A.—In a case of subarachnoid haemorrhage treated conservatively the risk of further haemorrhage is over 60%, and at the end of six months the risk will be only 10%.[1,2] The mortality from a second haemorrhage is 60%, and 75% if the patient survives this and the aneurysm bleeds again.[3] An arbitrary period of six months from the time of haemorrhage is, therefore, a reasonable time in which to anticipate a second attack.

References

1 Hyland, H. H., *Arch. Neurol. Psychiat. (Chicago)*, 1950, 63, 61.
2 Walton, J. N., *Brit. med. J.*, 1952, 2, 802.
3 McKissock, W., Richardson, A., and Walsh, L., *Lancet*, 1960, 1, 1203.

Paediatric Dentistry Under Hypnosis

Q.—*Is there any particular psychological danger in extracting children's teeth under hypnosis? Might the suppression of emotion lead to symptoms later on?*

A.—Little attention has been directed to the follow-up of cases of dental treatment in children in whom a hypnotic technique, either with or without anaesthesia, has been used. Emotional behaviour in association with dental extractions is related to the child's ability to tolerate facing new experience and discomfort, and is associated with fears about oral aggressiveness and about being overwhelmed by restraint or respiratory obstruction. Whether or not a child acts out this disturbance, there is a great need for a truly supportive relationship between the child and those in charge of the procedure to facilitate the expression of feelings and

fantasies so that the experience becomes a constructive and not a destructive one. If a hypnotic approach is being used it is possible to utilize the necessary interviews with the child before and after the procedure to promote this. It is, of course, well known that satisfactory analgesia cannot be achieved in all cases by the use of a hypnotic technique, and when suggestions of absence of pain have been unsuccessful insecurity in the dental situation must be increased. In actual fact, paediatric anaesthetists frequently use a hypnotic type of induction to general anaesthesia, although not all would use the term "hypnosis."

Inheritance of Ichthyosis

Q.—*Two young people planning to get married both suffer from ichthyosis. In addition, the boy suffers from asthma and eczema. The boy is the only case in his family but the girl has a history of ichthyosis down one side of her family. What are the possibilities of illness for the children of such a marriage?*

A.—There are probably two independent risks to children of this couple; a fairly high risk of inheriting ichthyosis vulgaris from the mother, and a small risk of inheriting the father's ichthyosis with asthma and eczema. Uncomplicated ichthyosis may be due to several different genes, but here, since it is present in a girl and in more than one generation of her family, the gene concerned is probably a dominant with a fairly high rate of manifestation. Ichthyosis in association with eczema and asthma, in many instances at least, appears to be due to an autosomal recessive gene and, though instances of transmission to a second generation are known, they are not the rule.[1]

REFERENCE

[1] Touraine, A., *L'Hérédité en Médecine*, 1955. Masson, Paris.

Vernal Conjunctivitis

Q.—*Vernal conjunctivitis, or spring catarrh, is frequently resistant to local cortisone therapy. I believe that some American authorities have claimed that lactic acid and adrenaline drops are of benefit—is this so and what is their composition? Is there any other treatment that stands a reasonable chance of success?*

A.—Cases of vernal conjunctivitis which do not respond to local cortisone may sometimes respond to systemic cortisone. β-radiation has been claimed to be of value, and mucous grafting to the denuded tarsal plate has been suggested. Pollen sensitivity can be demonstrated in some cases and good results have been claimed for specific desensitization. Prednisone has been found the most effective steroid.[1] The treatment with lactic acid was suggested by Barradah.[2] The drops contained 1–2% tetracaine hydrochloride, 1% of 1:1,000 epinephrine, and 1% lactic acid in distilled water. A full discussion of vernal conjunctivitis and its treatment can be found in a book by Beigelman.[3]

REFERENCES

[1] Neumann, E., *Brit. J. Ophthal.*, 1958, **42**, 674.
[2] Barradah, M. A. E., *Bull. ophthal. Soc. Egypt*, 1956, **49**, 115.
[3] Beigelman, M. N., *Vernal Conjunctivitis*, 1950. Los Angeles, University of Southern California Press.

Pregnancy Hazards in Radiographers

Q.—*Is it advisable for a married radiographer to stop work before becoming pregnant, or to stop work as soon as she becomes pregnant? She works a 36-hour week and her personal exposure disk readings vary from 0 to 15 milli-Roentgens per three weeks.*

A.—The recommendations of the International Commission on Radiological Protection do not debar women, including pregnant women, from following their normal occupation in radiology. Although the embryo, particularly at the period of morphogenesis in the early weeks of pregnancy, is highly radiosensitive and any damage is likely to result in morphological disorder, it is considered that the probability of induction of such morphological change by the very low doses now permitted in radiological occupations is so low that it can be neglected. It must be remembered that the proportion of all newborn infants that show spontaneously morphological deviation from what is taken to be normal is relatively high—some 5%. This high rate of natural aberration is due to manifestation of spontaneously occurring genetic mutation and to intrauterine environmental causes.

Since the dose-rate to which the radiographer in question is exposed is at maximum only some 5% of the permitted weekly dose for radiographers, there can be no compelling reason to advise her to give up her occupation before pregnancy occurs or after it is confirmed.

NOTES AND COMMENTS

Chest X-ray in Pregnancy.—Dr. G. R. Airth (Southmead Hospital, Bristol) writes: Would the author of the answer to this question ("Any Questions?" August 13, p. 551) be good enough to enlarge on his statement that the incidence of tuberculosis in young pregnant women is still about 2 per 1,000? Does he refer to tuberculosis of proven activity, or does he include the quiescent and apparently healed lesion? If all are included, the incidence may well be as stated; if active tubercle is being considered, I think that the incidence is very much smaller than 2 per 1,000. Having been instrumental in starting the chest radiography service in this area over 10 years ago, I am very concerned to find it so misused in 1960. At a time when the number of active tuberculous lesions was considerable, the intention was to segregate patients in an observation ward, away from uninfected maternity cases. I can find no evidence that any significant number of tuberculous lesions worsen during pregnancy, but it is common knowledge that they may do so after delivery. Very few lesions indeed are found initially by routine antenatal chest radiography—i.e., when the patient has no symptoms of chest disease. The logical time to examine the chest seems to be at a foetal age of 36 weeks or later, to provide early warning of danger to the baby or other mothers in a hospital ward, and of the need for close observation of the mother herself after delivery. I see no valid reason for chest *x*-ray examination early in pregnancy.

Our Expert replies: The last Ministry of Health report from the mass radiography units examining women during the antenatal period found the incidence of active tuberculosis requiring treatment at 1.6 per 1,000. Another 1.6 per 1,000 were found to require careful supervision in the chest clinics.

Corrections.—The last five lines of the paper by Drs. David Phear and William C. Walker (October 1, p. 995) should have read as follows: "However, in a recent trial of β-phenylisopropyl-hydrazine ('cavodil') MacKinnon *et al.* (1960) found worthwhile improvement of angina. Our experience has been less encouraging. Hepatic damage with jaundice developed in one of 12 patients treated with cavodil."

We much regret a printing error in the second paragraph of the summary of the paper entitled "Disinfection of the Skin of Operation Sites" by Dr. E. J. L. Lowbury, Mr. H. A. Lilly, and Dr. J. P. Bull (*Journal*, October 8, p. 1039). We printed "Iodine 1% in alcohol had approximately the same effect. . . ." This should have read "Iodine 1% in alcohol and chlorhexidine (0.5%) in alcohol had approximately the same effect. . ."

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The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

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